```
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 NEWS  1           Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2           "Ask CAS" for self-help around the clock
 NEWS  3  SEP 01   New pricing for the Save Answers for SciFinder Wizard within
                   STN Express with Discover!
 NEWS  4  OCT 28   KOREAPAT now available on STN
 NEWS  5  NOV 30   PHAR reloaded with additional data
 NEWS  6  DEC 01   LISA now available on STN
 NEWS  7  DEC 09   12 databases to be removed from STN on December 31, 2004
 NEWS  8  DEC 15   MEDLINE update schedule for December 2004
 NEWS  9  DEC 17   ELCOM reloaded; updating to resume; current-awareness
                   alerts (SDIs) affected
 NEWS  10 DEC 17   COMPUAB reloaded; updating to resume; current-awareness
                   alerts (SDIs) affected
 NEWS  11 DEC 17   SOLIDSTATE reloaded; updating to resume; current-awareness
                   alerts (SDIs) affected
 NEWS  12 DEC 17   CERAB reloaded; updating to resume; current-awareness
                   alerts (SDIs) affected
 NEWS  13 DEC 17   THREE NEW FIELDS ADDED TO IFIPAT/IFIUDB/IFICDB
 NEWS  14 DEC 30   EPFULL: New patent full text database to be available on STN
 NEWS  15 DEC 30   CAPLUS - PATENT COVERAGE EXPANDED
 NEWS  16 JAN 03   No connect-hour charges in EPFULL during January and
                   February 2005
 NEWS  17 FEB 25   CA/CAPLUS - Russian Agency for Patents and Trademarks
                   (ROSPATENT) added to list of core patent offices covered
 NEWS  18 FEB 10   STN Patent Forums to be held in March 2005
 NEWS  19 FEB 16   STN User Update to be held in conjunction with the 229th ACS
                   National Meeting on March 13, 2005
 NEWS  20 FEB 28   PATDPAFULL - New display fields provide for legal status
                   data from INPADOC
 NEWS  21 FEB 28   BABS - Current-awareness alerts (SDIs) available
 NEWS  22 FEB 28   MEDLINE/LMEDLINE reloaded
 NEWS  23 MAR 02   GBFULL: New full-text patent database on STN
 NEWS  24 MAR 03   REGISTRY/ZREGISTRY - Sequence annotations enhanced

 NEWS EXPRESS  JANUARY 10 CURRENT WINDOWS VERSION IS V7.01a, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 10 JANUARY 2005

 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
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 NEWS WWW      CAS World Wide Web Site (general information)

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* * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 15:17:55 ON 03 MAR 2005

=> fil reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 15:18:07 ON 03 MAR 2005
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 2 MAR 2005 HIGHEST RN 841200-41-7
DICTIONARY FILE UPDATES: 2 MAR 2005 HIGHEST RN 841200-41-7

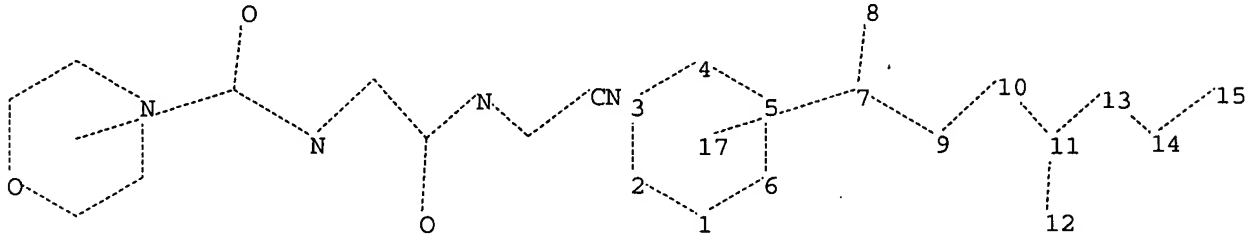
TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
Uploading C:\Program Files\Stnexp\Queries\10758893.str

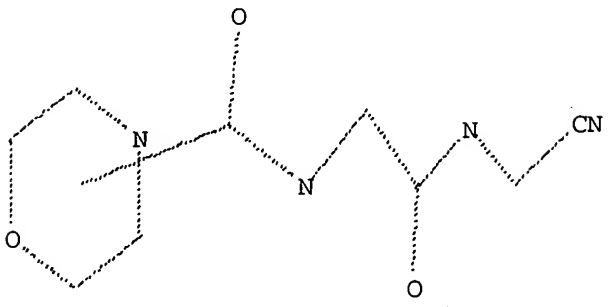


chain nodes :
7 8 9 10 11 12 13 14 15
ring nodes :
1 2 3 4 5 6
chain bonds :
7-8 7-9 9-10 10-11 11-12 11-13 13-14 14-15
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6
exact/norm bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-9 9-10 10-11 11-12 11-13 13-14 14-15
isolated ring systems :
containing 1 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS
11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 17:CLASS

L1 STRUCTURE UPLOADED

=> d
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1
SAMPLE SEARCH INITIATED 15:18:30 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 28 TO ITERATE

100.0% PROCESSED 28 ITERATIONS 5 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 243 TO 877
PROJECTED ANSWERS: 5 TO 234

L2 5 SEA SSS SAM L1

=> s l1 full
FULL SEARCH INITIATED 15:18:33 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 478 TO ITERATE

100.0% PROCESSED 478 ITERATIONS 79 ANSWERS
SEARCH TIME: 00.00.01

L3 79 SEA SSS FUL L1

=> s l3 and caplus/lc
44463264 CAPLUS/LC
L4 79 L3 AND CAPLUS/LC

=> fil caplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 165.93 166.14

FILE 'CAPLUS' ENTERED AT 15:18:42 ON 03 MAR 2005
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FILE COVERS 1907 - 3 Mar 2005 VOL 142 ISS 10
FILE LAST UPDATED: 2 Mar 2005 (20050302/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

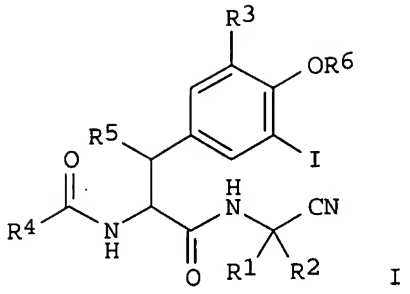
=> s l4
L5 9 L4

=> d ibib abs hitstr 1-9

L5 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:267319 CAPLUS
DOCUMENT NUMBER: 140:304079
TITLE: Preparation of iodotyrosine cyanomethylamides as Cathepsin B inhibitors
INVENTOR(S): Burrill, Leland C., II; Palmer, James T.; Rydzewski, Robert M.
PATENT ASSIGNEE(S): Axys Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004026851	A1	20040401	WO 2003-US29545	20030916
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 2002-412368P P 20020920
OTHER SOURCE(S): MARPAT 140:304079
GI



I

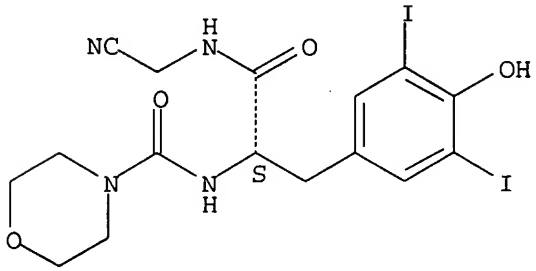
AB Title compds. [I; R1, R2 = H, alkyl, haloalkyl, hydroxyalkyl, aryl, aralkyl; R1R2 = atoms to form a cycloalkyl, heterocycloalkyl ring; R3 = alkyl, iodo; R4 = (substituted) aryl, heteroaryl, heterocycloalkyl; R5, R6 = H, alkyl], were prepared as Cathepsin B inhibitors (no data). Thus, 4-morpholinobenzoic acid hydrochloride, hydroxybenzotriazole, Et3N, and EDC were stirred 30 min in DMF; L-3,5-diiodotyrosine, Et3N, and H2O in DMF were added followed by stirring for 16 h to give (S)-3-(4-hydroxy-3,5-diiodophenyl)-2-(4-morpholin-4-ylbenzoylamino)propionic acid. The latter was stirred overnight with aminoacetonitrile hydrochloride, HBTU, and N-methylmorpholine in DMF to give (S)-N-[1-(cyanomethylcarbamoyl)-2-(4-hydroxy-3,5-diiodophenyl)ethyl]-4-morpholin-4-ylbenzamide.

IT **676477-50-2P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of iodotyrosine cyanomethylamides as Cathepsin B inhibitors)

RN 676477-50-2 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-2-[(cyanomethyl)amino]-1-[(4-hydroxy-3,5-diiodophenyl)methyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:55370 CAPLUS

DOCUMENT NUMBER: 140:5280

TITLE: Design and synthesis of dipeptide nitriles as reversible and potent Cathepsin S inhibitors. [Erratum to document cited in CA138:56234]

AUTHOR(S): Ward, Yancey D.; Thomson, David S.; Frye, Leah L.; Cywin, Charles L.; Morwick, Tina; Emmanuel, Michel J.; Zindell, Renee; McNeil, Daniel; Bekkali, Younes; Girardot, Marc; Hrapchak, Matt; DeTuri, Molly; Crane, Kathy; White, Della; Pav, Susan; Wang, Yong; Hao, Ming-Hong; Grygon, Christine A.; Labadia, Mark E.; Freeman, Dorothy M.; Davidson, Walter; Hopkins, Jerry

L.; Brown, Maryanne L.; Spero, Denice M.
CORPORATE SOURCE: Boehringer Ingelheim Pharmaceuticals, Ridgefield, CT, 06877-0368, USA
SOURCE: Journal of Medicinal Chemistry (2003), 46(5), 882
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The name of author Marc Girardot was incorrect in the version published on the Web 10/31/2002 (ASAP) and in the Dec. 5, 2002 issue (Volume 45, Number 25, pp 5471-5482). The correct electronic version of the manuscript was published on 01/20/2003.

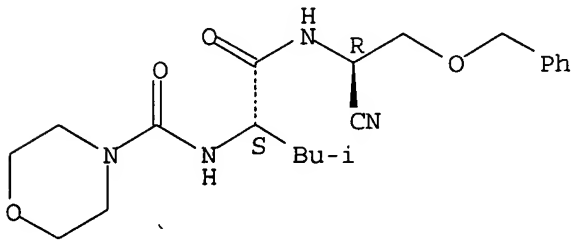
IT **479091-78-6**
RL: PRP (Properties)
(crystal structure of cathepsin S cocrystd. with dipeptide nitrile as its reversible inhibitor (Erratum))

RN 479091-78-6 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-1-cyano-2-(phenylmethoxy)ethyl]amino]carbonyl]-3-methylbutyl]-, compd. with cathepsin S (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 290816-77-2
CMF C21 H30 N4 O4

Absolute stereochemistry.



CM 2

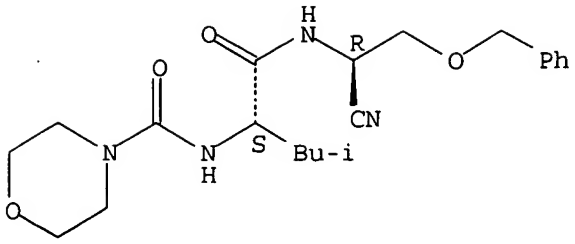
CRN 71965-46-3
CMF Unspecified
CCI MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **290816-77-2P**
RL: BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and biol. activity of dipeptide nitriles as reversible and potent cathepsin S inhibitors (Erratum))

RN 290816-77-2 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-1-cyano-2-(phenylmethoxy)ethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

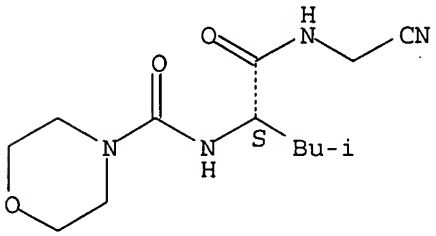
Absolute stereochemistry.



IT **225119-70-0P 290816-49-8P 290816-76-1P**
290816-78-3P 290816-82-9P 290816-83-0P
290816-89-6P 290816-91-0P 290817-01-5P
290817-02-6P 290817-03-7P 290817-12-8P
479091-50-4P 479091-51-5P 479091-52-6P
479091-53-7P 479091-54-8P 479091-55-9P
479091-56-0P 479091-57-1P 479091-58-2P
479091-59-3P 479091-60-6P 479091-61-7P
479091-62-8P 479091-63-9P 479091-64-0P
479091-65-1P 479091-66-2P 479091-67-3P
479091-68-4P 479091-69-5P
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and biol. activity of dipeptide nitriles as reversible and potent cathepsin S inhibitors (Erratum))

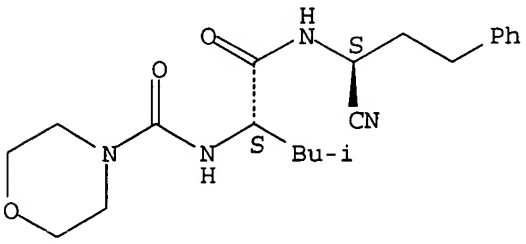
RN 225119-70-0 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



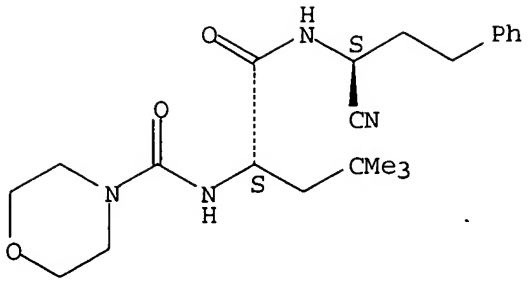
RN 290816-49-8 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyano-3-phenylpropyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



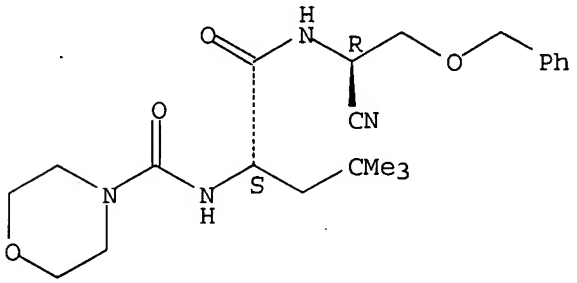
RN 290816-76-1 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyano-3-phenylpropyl]amino]carbonyl]-3,3-dimethylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



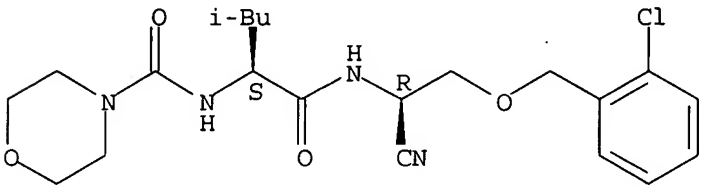
RN 290816-78-3 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-1-cyano-2-(phenylmethoxy)ethyl]amino]carbonyl]-3,3-dimethylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



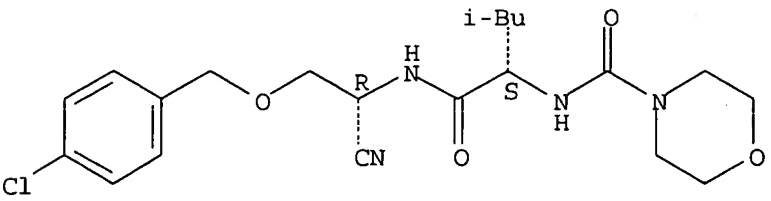
RN 290816-82-9 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-2-[(2-chlorophenyl)methoxy]-1-cyanoethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



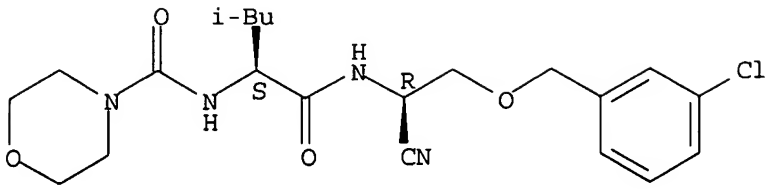
RN 290816-83-0 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-2-[(4-chlorophenyl)methoxy]-1-cyanoethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



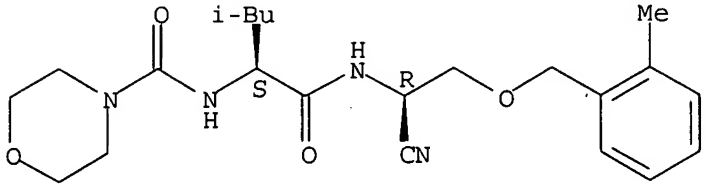
RN 290816-89-6 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-2-[(3-chlorophenyl)methoxy]-1-cyanoethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



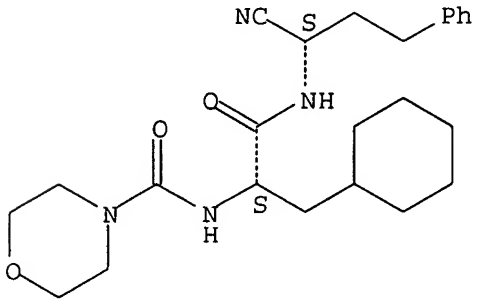
RN 290816-91-0 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-1-cyano-2-[(2-methylphenyl)methoxy]ethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



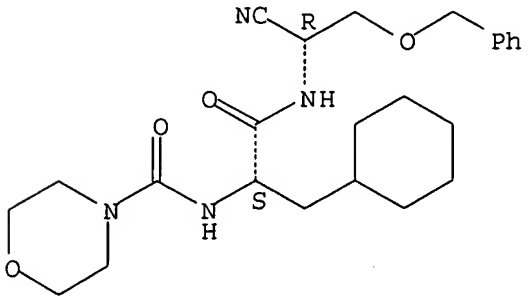
RN 290817-01-5 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-2-[[(1S)-1-cyano-3-phenylpropyl]amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



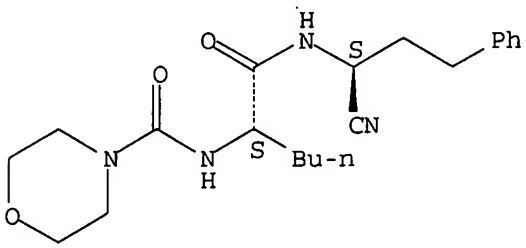
RN 290817-02-6 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-2-[[(1R)-1-cyano-2-(phenylmethoxy)ethyl]amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



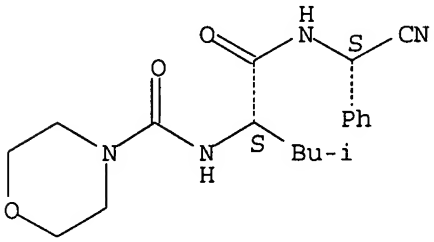
RN 290817-03-7 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyano-3-phenylpropyl]amino]carbonyl]pentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



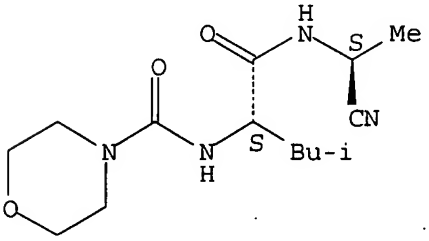
RN 290817-12-8 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(S)-cyanophenylmethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



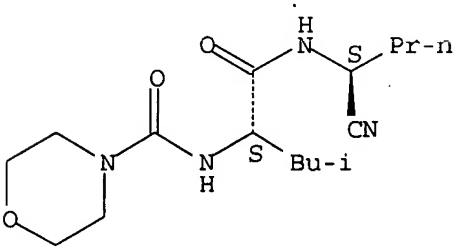
RN 479091-50-4 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyanoethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



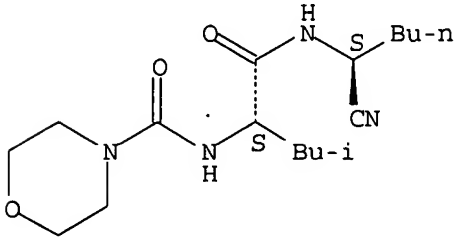
RN 479091-51-5 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyanobutyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



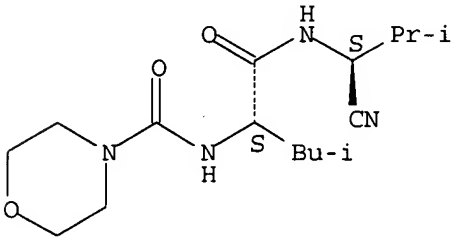
RN 479091-52-6 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyanopentyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



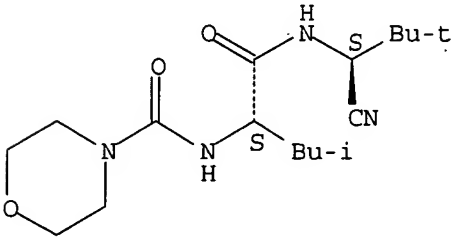
RN 479091-53-7 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyano-2-methylpropyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



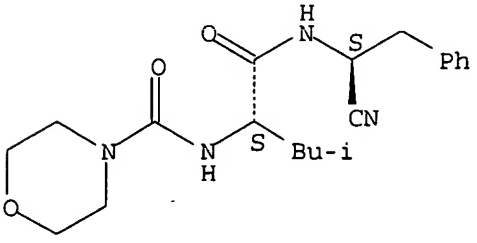
RN 479091-54-8 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyano-2,2-dimethylpropyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



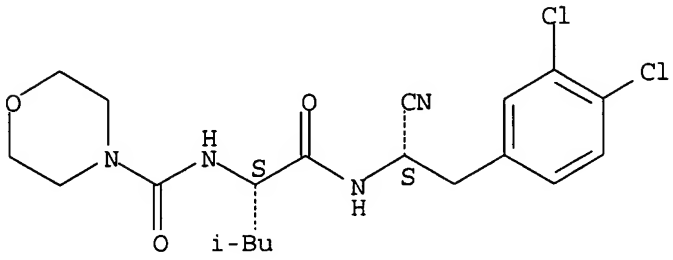
RN 479091-55-9 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyano-2-phenylethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



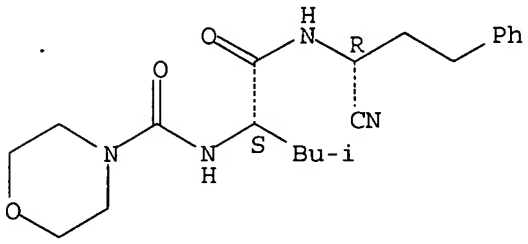
RN 479091-56-0 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyano-2-(3,4-dichlorophenyl)ethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



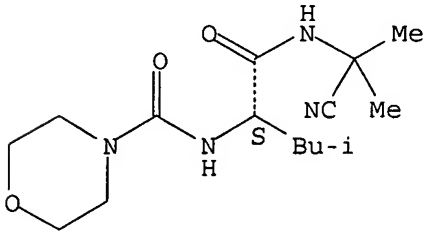
RN 479091-57-1 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-1-cyano-3-phenylpropyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



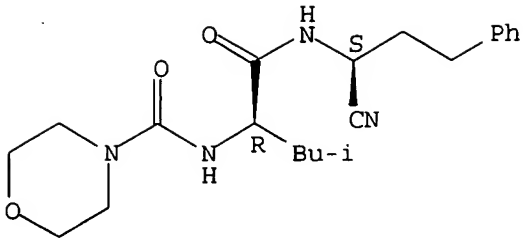
RN 479091-58-2 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[(1-cyano-1-methylethyl)amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



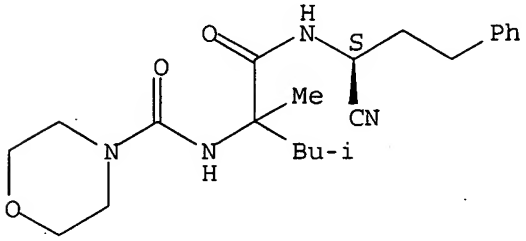
RN 479091-59-3 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1R)-1-[[[(1S)-1-cyano-3-phenylpropyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



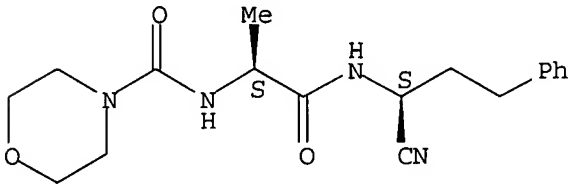
RN 479091-60-6 CAPLUS
CN 4-Morpholinecarboxamide, N-[1-[[[(1S)-1-cyano-3-phenylpropyl]amino]carbonyl]-1,3-dimethylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



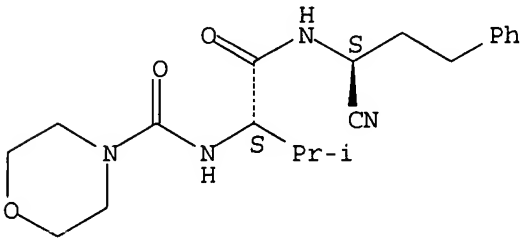
RN 479091-61-7 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-2-[[(1S)-1-cyano-3-phenylpropyl]amino]-1-methyl-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



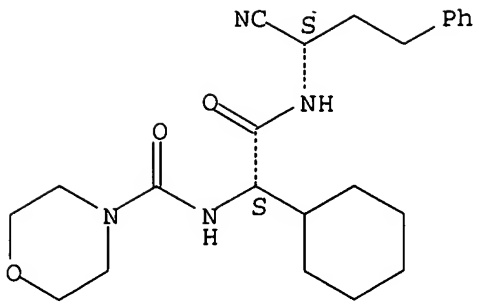
RN 479091-62-8 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyano-3-phenylpropyl]amino]carbonyl]-2-methylpropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



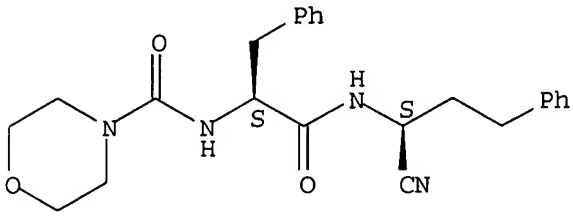
RN 479091-63-9 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-2-[[(1S)-1-cyano-3-phenylpropyl]amino]-1-cyclohexyl-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



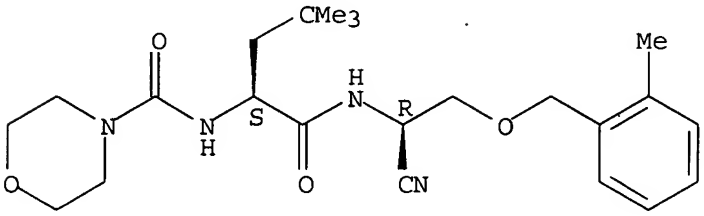
RN 479091-64-0 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-2-[[(1S)-1-cyano-3-phenylpropyl]amino]-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



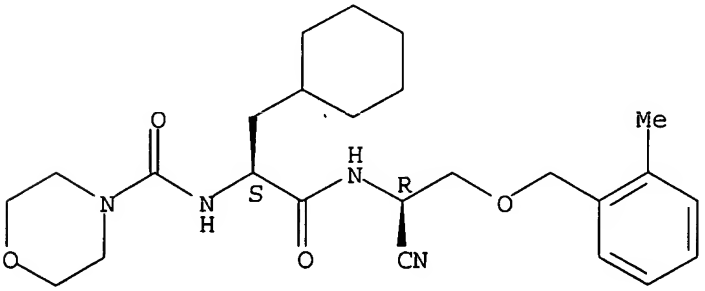
RN 479091-65-1 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-1-cyano-2-[(2-methylphenyl)methoxy]ethyl]amino]carbonyl]-3,3-dimethylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



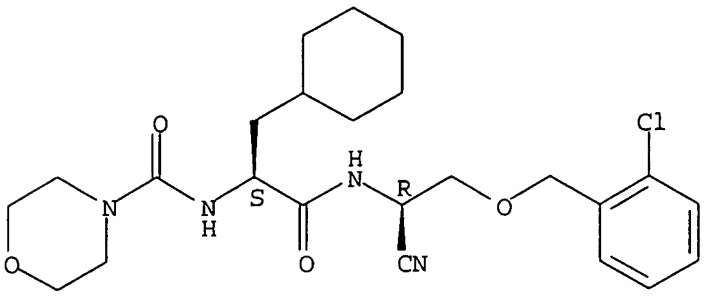
RN 479091-66-2 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-2-[[(1R)-1-cyano-2-[(2-methylphenyl)methoxy]ethyl]amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



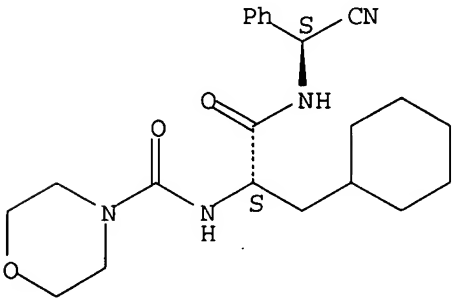
RN 479091-67-3 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-2-[[(1R)-2-[(2-chlorophenyl)methoxy]-1-cyanoethyl]amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



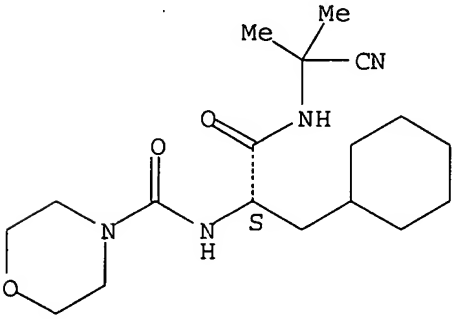
RN 479091-68-4 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-2-[[(S)-cyanophenylmethyl]amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 479091-69-5 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-2-[(1-cyano-1-methylethyl)amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L5 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:835002 CAPLUS
DOCUMENT NUMBER: 138:56234
TITLE: Design and synthesis of dipeptide nitriles as reversible and potent cathepsin S inhibitors
AUTHOR(S): Ward, Yancey D.; Thomson, David S.; Frye, Leah L.; Cywin, Charles L.; Morwick, Tina; Emmanuel, Michel J.; Zindell, Renee; McNeil, Daniel; Bekkali, Younes;

Giradot, Marc; Hrapchak, Matt; DeTuri, Molly; Crane, Kathy; White, Della; Pav, Susan; Wang, Yong; Hao, Ming-Hong; Grygon, Christine A.; Labadia, Mark E.; Freeman, Dorothy M.; Davidson, Walter; Hopkins, Jerry L.; Brown, Maryanne L.; Spero, Denice M.
CORPORATE SOURCE: Boehringer Ingelheim Pharmaceuticals, Ridgefield, CT, 06877-0368, USA
SOURCE: Journal of Medicinal Chemistry (2002), 45(25), 5471-5482
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:56234
AB The specificity of the immune response relies on processing of foreign proteins and presentation of antigenic peptides at the cell surface. Inhibition of antigen presentation, and the subsequent activation of T-cells, should, in theory, modulate the immune response. The cysteine protease cathepsin S performs a fundamental step in antigen presentation and therefore represents an attractive target for inhibition. Herein, the authors report a series of potent and reversible Cathepsin S inhibitors based on dipeptide nitriles. These inhibitors show nanomolar inhibition of the target enzyme as well as cellular potency in a human B cell line. The first x-ray crystal structure of a reversible inhibitor cocrystd. with cathepsin S is also reported.

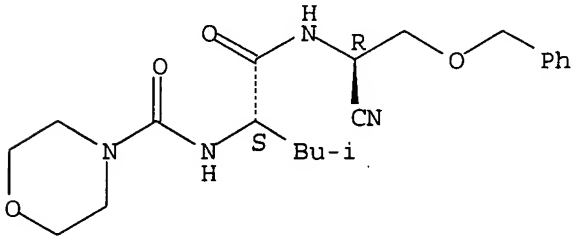
IT **479091-78-6**
RL: PRP (Properties)
(crystal structure of cathepsin S cocrystd. with a dipeptide nitrile as its reversible inhibitor)

RN 479091-78-6 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-1-cyano-2-(phenylmethoxy)ethyl]amino]carbonyl]-3-methylbutyl]-, compd. with cathepsin S (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 290816-77-2
CMF C21 H30 N4 O4

Absolute stereochemistry.



CM 2

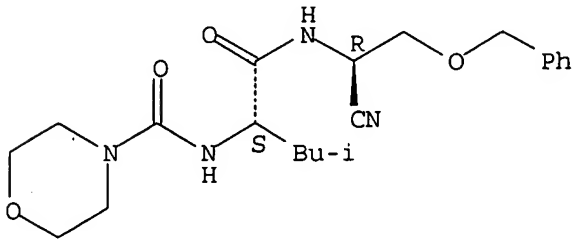
CRN 71965-46-3
CMF Unspecified
CCI MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **290816-77-2P**
RL: BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and biol. activity of dipeptide nitriles as reversible and potent cathepsin S inhibitors)

RN 290816-77-2 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-1-cyano-2-(phenylmethoxy)ethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

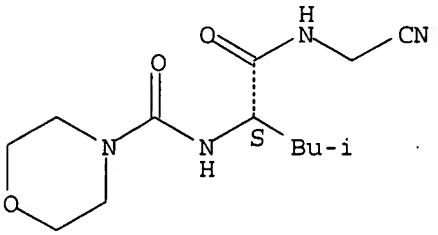
Absolute stereochemistry.



IT **225119-70-0P 290816-49-8P 290816-76-1P**
290816-78-3P 290816-82-9P 290816-83-0P
290816-89-6P 290816-91-0P 290817-01-5P
290817-02-6P 290817-03-7P 290817-12-8P
479091-50-4P 479091-51-5P 479091-52-6P
479091-53-7P 479091-54-8P 479091-55-9P
479091-56-0P 479091-57-1P 479091-58-2P
479091-59-3P 479091-60-6P 479091-61-7P
479091-62-8P 479091-63-9P 479091-64-0P
479091-65-1P 479091-66-2P 479091-67-3P
479091-68-4P 479091-69-5P
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and biol. activity of dipeptide nitriles as reversible and potent cathepsin S inhibitors)

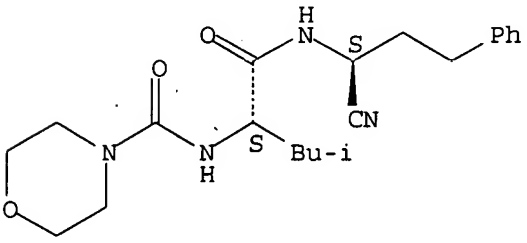
RN 225119-70-0 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



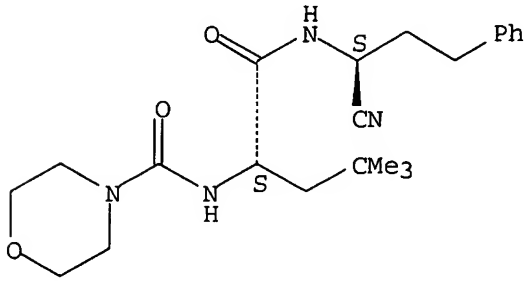
RN 290816-49-8 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyano-3-phenylpropyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



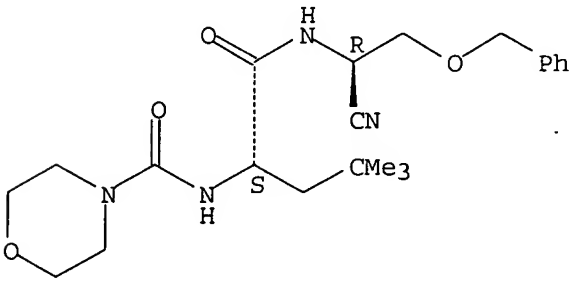
RN 290816-76-1 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyano-3-phenylpropyl]amino]carbonyl]-3,3-dimethylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



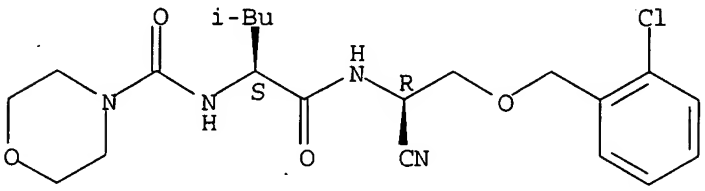
RN 290816-78-3 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-1-cyano-2-(phenylmethoxy)ethyl]amino]carbonyl]-3,3-dimethylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



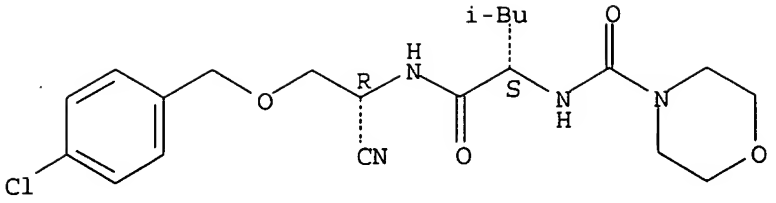
RN 290816-82-9 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-2-[(2-chlorophenyl)methoxy]-1-cyanoethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



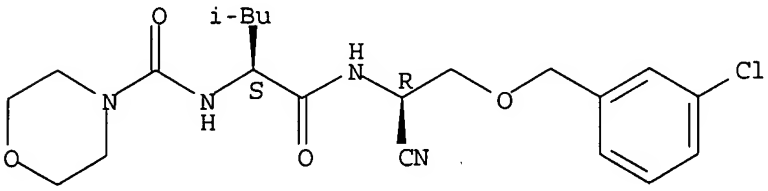
RN 290816-83-0 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-2-[(4-chlorophenyl)methoxy]-1-cyanoethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



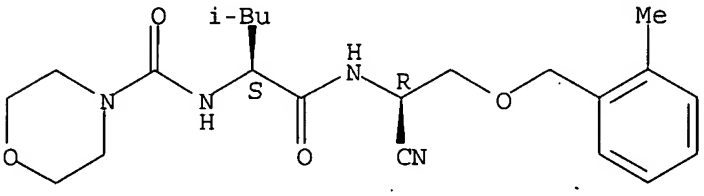
RN 290816-89-6 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-2-[(3-chlorophenyl)methoxy]-1-cyanoethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



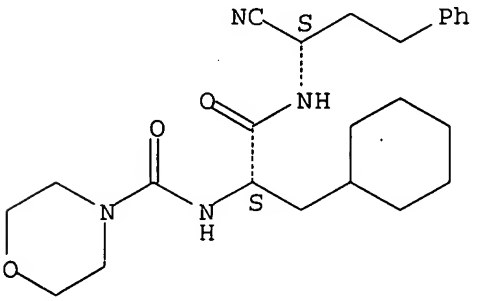
RN 290816-91-0 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-1-cyano-2-[(2-methylphenyl)methoxy]ethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



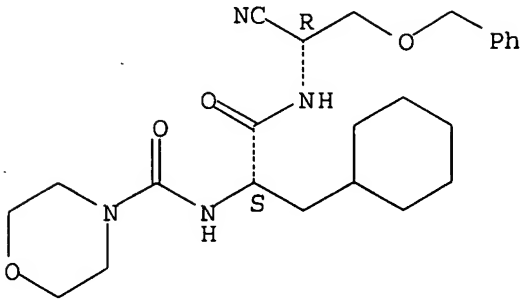
RN 290817-01-5 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-2-[[(1S)-1-cyano-3-phenylpropyl]amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



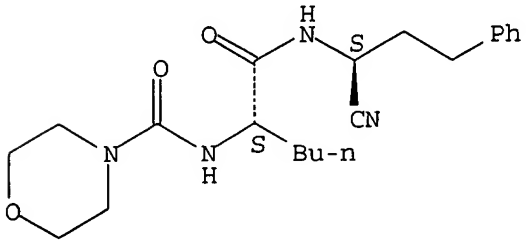
RN 290817-02-6 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-2-[[(1R)-1-cyano-2-(phenylmethoxy)ethyl]amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



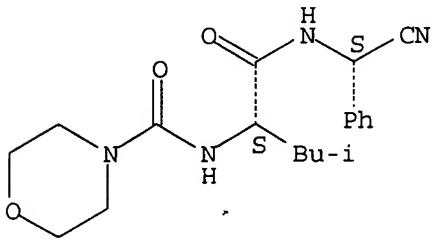
RN 290817-03-7 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyano-3-phenylpropyl]amino]carbonyl]pentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



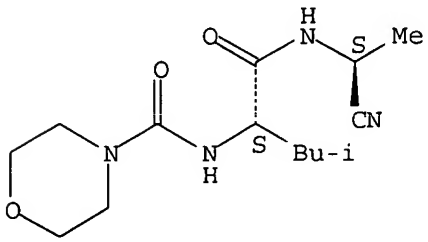
RN 290817-12-8 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(S)-cyanophenylmethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 479091-50-4 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyanoethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

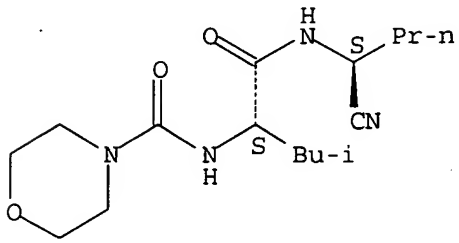
Absolute stereochemistry.



RN 479091-51-5 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyanobutyl]amino]carbonyl]-3-

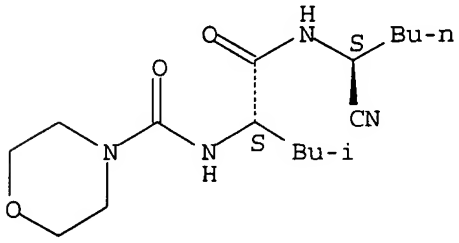
methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



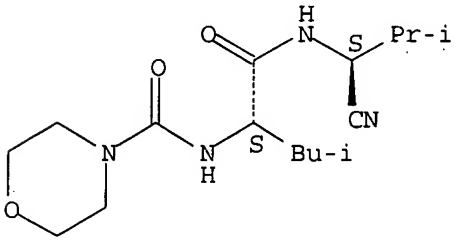
RN 479091-52-6 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyanopentyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



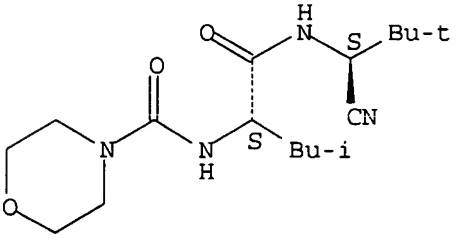
RN 479091-53-7 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyano-2-methylpropyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 479091-54-8 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyano-2,2-dimethylpropyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

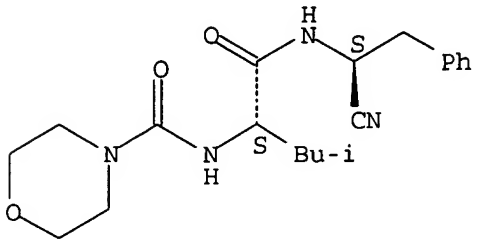
Absolute stereochemistry.



RN 479091-55-9 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyano-2-

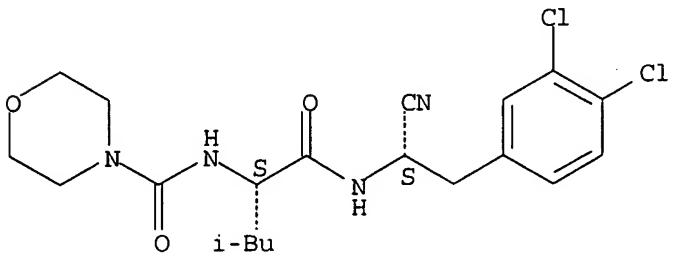
phenylethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



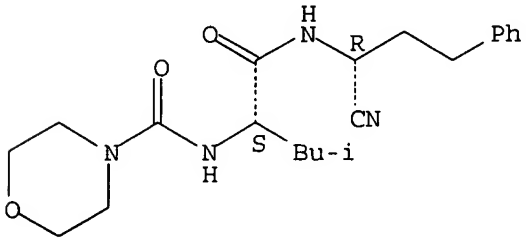
RN 479091-56-0 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyano-2-(3,4-dichlorophenyl)ethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



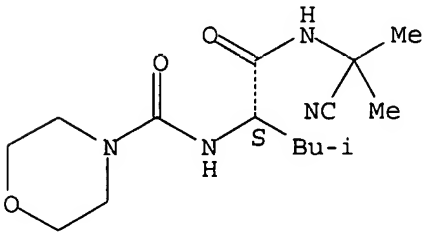
RN 479091-57-1 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-1-cyano-3-phenylpropyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



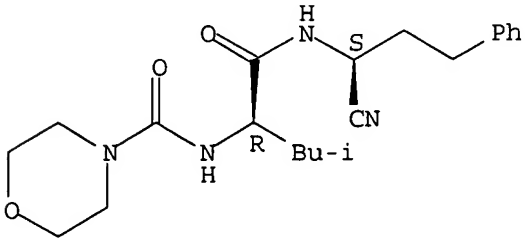
RN 479091-58-2 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[(1-cyano-1-methylethyl)amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



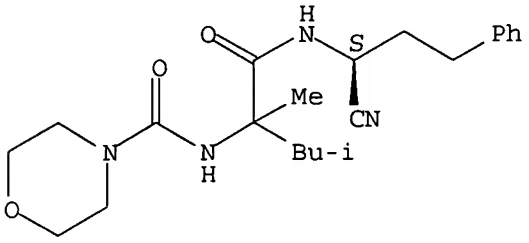
RN 479091-59-3 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1R)-1-[[[(1S)-1-cyano-3-phenylpropyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



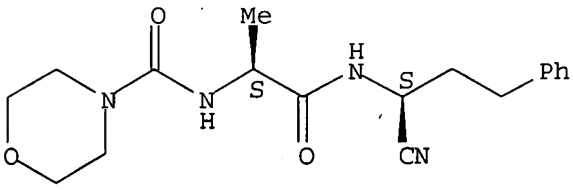
RN 479091-60-6 CAPLUS
CN 4-Morpholinecarboxamide, N-[1-[[[(1S)-1-cyano-3-phenylpropyl]amino]carbonyl]-1,3-dimethylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



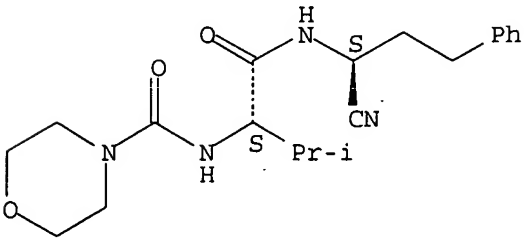
RN 479091-61-7 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-2-[[(1S)-1-cyano-3-phenylpropyl]amino]-1-methyl-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 479091-62-8 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyano-3-phenylpropyl]amino]carbonyl]-2-methylpropyl]- (9CI) (CA INDEX NAME)

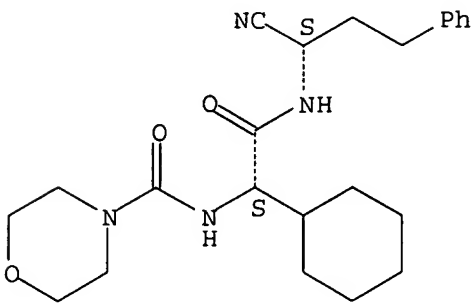
Absolute stereochemistry.



RN 479091-63-9 CAPLUS

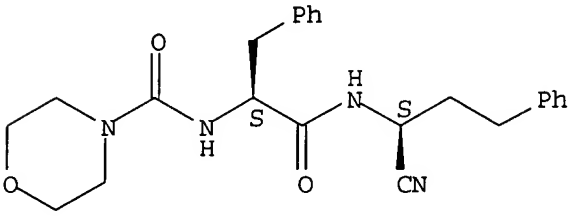
CN 4-Morpholinecarboxamide, N-[(1S)-2-[[(1S)-1-cyano-3-phenylpropyl]amino]-1-cyclohexyl-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



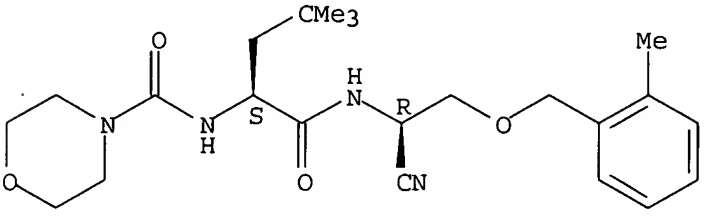
RN 479091-64-0 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-2-[[(1S)-1-cyano-3-phenylpropyl]amino]-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



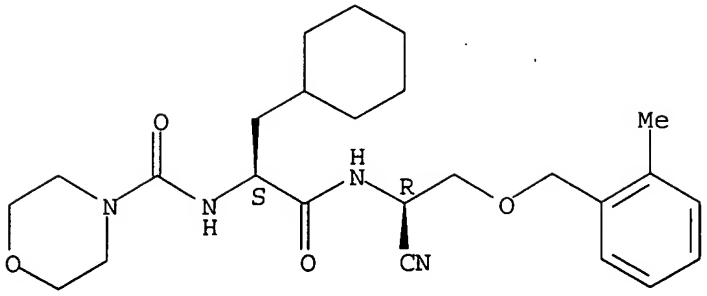
RN 479091-65-1 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-1-cyano-2-[(2-methylphenyl)methoxy]ethyl]amino]carbonyl]-3,3-dimethylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



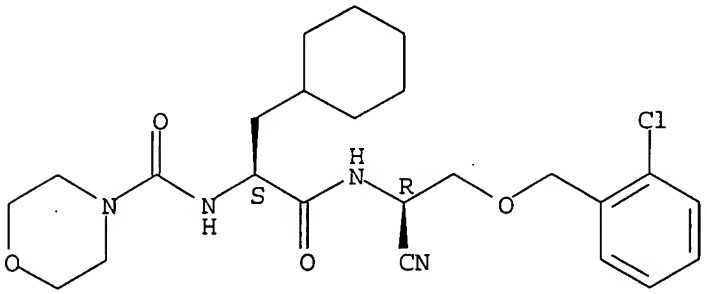
RN 479091-66-2 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-2-[[(1R)-1-cyano-2-[(2-methylphenyl)methoxy]ethyl]amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



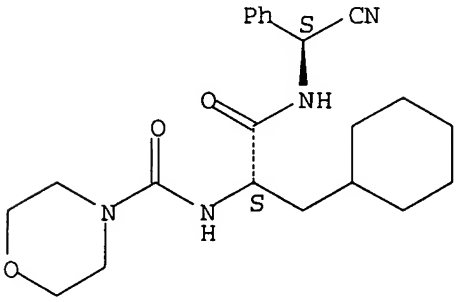
RN 479091-67-3 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-2-[[(1R)-2-[(2-chlorophenyl)methoxy]-1-cyanoethyl]amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



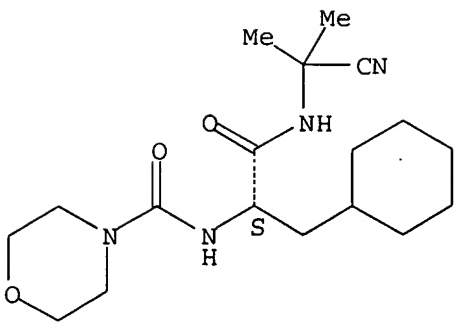
RN 479091-68-4 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-2-[[(S)-cyanophenylmethyl]amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 479091-69-5 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-2-[(1-cyano-1-methylethyl)amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

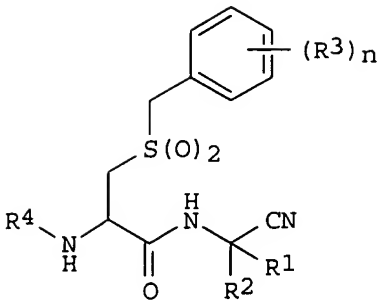


L5 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:208258 CAPLUS
DOCUMENT NUMBER: 134:237310
TITLE: Preparation and use of 2-aminoacyl-3-benzylsulfonylpropionamide derivatives as as cathepsin S inhibitors
INVENTOR(S): Graupe, Michael; Link, John O.; Patterson, John W.; Zipfel, Sheila
PATENT ASSIGNEE(S): Axys Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 90 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001019808	A1	20010322	WO 2000-US25341	20000915
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6492362	B1	20021210	US 2000-663449	20000915
US 2004014796	A1	20040122	US 2002-256354	20020927

PRIORITY APPLN. INFO.:
US 1999-154245P P 19990916
US 1999-171831P P 19991222
US 2000-224552P P 20000810
US 2000-663449 A3 20000915

OTHER SOURCE(S): MARPAT 134:237310
GI



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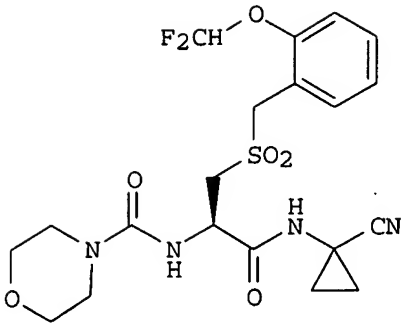


II

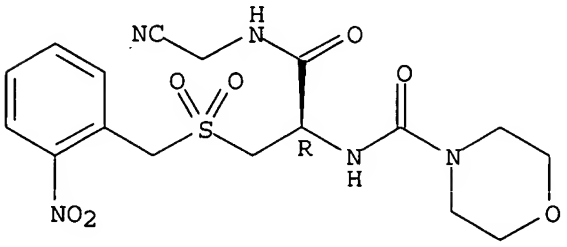
AB Compds. of formula I are claimed [wherein; n is 1-5, R1 is H and R2 is cyano, C5-heteroaryl or R1 and R2 are H, halo, alkyl, alkyl, X1OR5 where X1 and R5 are defined below or R1 and R2 together with the carbon atom, are (hetero)cycloalkylene; R3 is, at the first occurrence, NO2, CF3O, CHF2O, X1NR5R5, X1C(O)NR5R5, X1SR5, etc., where X1 is a bond or alkylene, R5 is H or (substituted)alkyl; R3 is at each other occurrence, is H, alkyl, CN, halo, etc.; R4 is C(O)X2R8 or S(O)2X2R8, where X2 is a bond, O or N(H or alkyl) and R8 is (substituted)alkyl, (hetero)cycloalkyl, substituted heteroaryl, etc.]. Preparation of I proceeds by one of four routes. The cyanomethyl amide side-chain may be formed by condensation of a cyanomethylamine with the parent carboxylic acid (optionally as the sulfide analog, followed by oxidation to the sulfone). The R4-NH bond may be formed by alkylation of the parent amine salt with R4L where L is a leaving group, or by addition of an amine to the corresponding isocyanate. Alternatively, the thiol-derived parent may be S-benzylated and oxidized to give compds. I. Compound II was prepared by amidation of (R)-3-[2-(difluoromethoxy)benzylsulfonyl]-2-[(1-morpholin-4-ylmethanoyl)amino]propionic acid with (1-aminocyclopropane)carbonitrile. Seventy examples of compds. I were provided. I showed Ki against cathepsin S activity in the range of 10-10 to 10-7 M. I inhibited cathepsin K 50-fold less than cathepsin S. Claimed uses of I are treatment of diseases which inhibition of cathepsin S can prevent.

IT **330474-09-4P 330474-81-2P 330665-93-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and use of 2-aminoacyl-3-benzylsulfonylpropionamide derivs. as selective cathepsin S inhibitors)

RN 330474-09-4 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1R)-2-[(cyanomethyl)amino]-1-[[[(2-nitrophenyl)methyl]sulfonyl]methyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

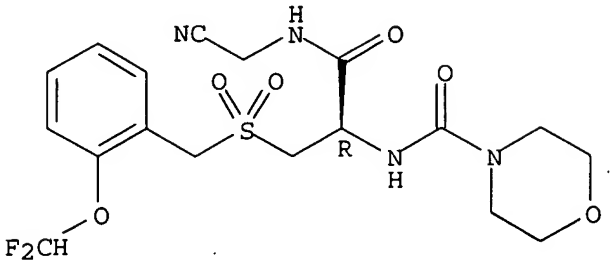
Absolute stereochemistry.



RN 330474-81-2 CAPLUS

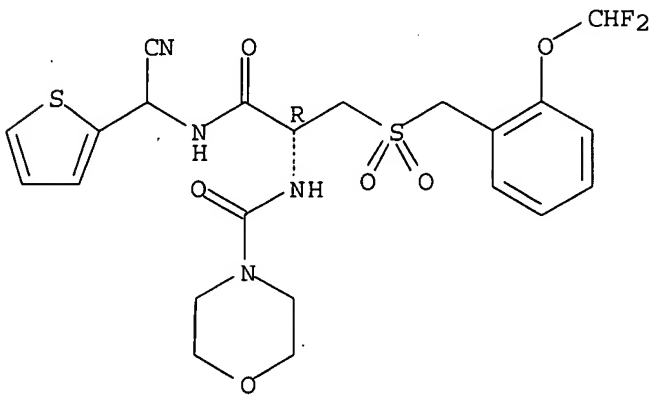
CN 4-Morpholinecarboxamide, N-[(1R)-2-[(cyanomethyl)amino]-1-[[[[2-(difluoromethoxy)phenyl]methyl]sulfonyl]methyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



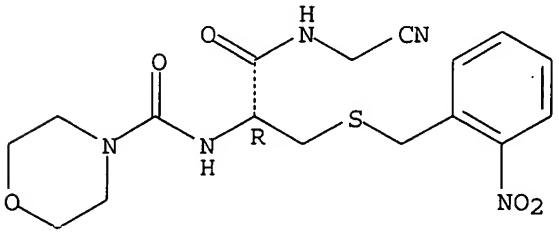
RN 330665-93-5 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1R)-2-[(cyano-2-thienylmethyl)amino]-1-[[[[2-(difluoromethoxy)phenyl]methyl]sulfonyl]methyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



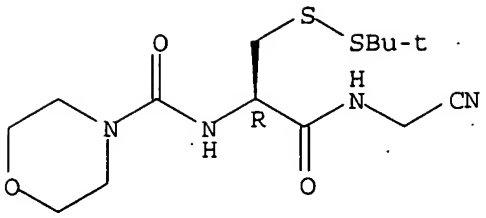
IT **294642-00-5P 330475-53-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and use of 2-aminoacyl-3-benzylsulfonylpropionamide derivs. as selective cathepsin S inhibitors)
RN 294642-00-5 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1R)-2-[(cyanomethyl)amino]-1-[[[(2-nitrophenyl)methyl]thio]methyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 330475-53-1 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1R)-2-[(cyanomethyl)amino]-1-[[(1,1-dimethylethyl)dithio]methyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:208246 CAPLUS
DOCUMENT NUMBER: 134:237830
TITLE: Preparation of amino acid cyanomethyl amides as cathepsin S inhibitors
INVENTOR(S): Graupe, Michael; Link, John O.; Patterson, John W.; Zipfel, Sheila
PATENT ASSIGNEE(S): Axys Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 261 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001019796	A1	20010322	WO 2000-US25415	20000915
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2384974	AA	20010322	CA 2000-2384974	20000915
EP 1212302	A1	20020612	EP 2000-966734	20000915
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
US 6492362	B1	20021210	US 2000-663449	20000915
JP 2003509410	T2	20030311	JP 2001-523376	20000915
AU 777472	B2	20041021	AU 2000-77033	20000915
US 2004014796	A1	20040122	US 2002-256354	20020927
PRIORITY APPLN. INFO.:			US 1999-154245P	P 19990916
			US 1999-171831P	P 19991222
			US 2000-224552P	P 20000810
			US 2000-663449	A3 20000915
			WO 2000-US25415	W 20000915

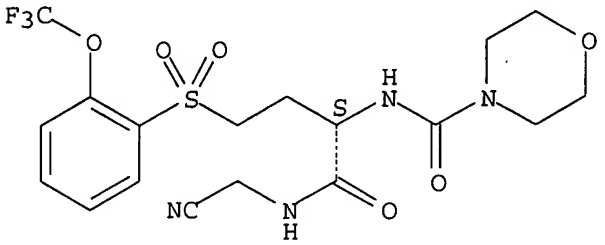
OTHER SOURCE(S): MARPAT 134:237830
AB R4NHCH(X1SO2X2R3)CONHCR1R2CN [X1, X2 = CH2, or X1 = CH2CH2 and X2 = bond; R1 = H, R2 = cyano, heteroaryl, alkylheteroaryl, or R1, R2 = H, halo, alkyl, X3OR9; R1R2C = cycloalkylene, heterocycloalkylene; R3 = (substituted) CHR5:CHR6, CR7:NR8; R5R6 = atoms to form alkenyl, cycloalkenyl, heterocycloalkenyl, aryl, heteroaryl, etc.; R7R8 = atoms to form heterocycloalkenyl, heteroaryl, heterobicycloaryl; R4 = COX4R11, SO2X4R11; X4 = bond, O, NR12; R12 = H, alkyl; R11 = (substituted) alkyl, cycloalkylalkyl, heterocycloalkylalkyl, etc.; R9 = H, alkyl, haloalkyl; X3 = bond, alkylene], were prepared Thus, 2R-benzoylamino-3-(4-methylbenzylsulfanyl)propionic acid (preparation given), EDCI, HOBt,

aminoacetonitrile bisulfate, and N-methylmorpholine were stirred together in N-methylpyrrolidinone for 5 h to give N-[1R-cyanomethylcarbamoyl-2-(4-methylbenzylsulfanyl)ethyl]benzamide. This was stirred with oxone in MeOH for 16 h to give N-[(R)-1-(cyanomethylcarbamoyl)-2-p-tolylmethanesulfonylethyl]benzamide. Title compds. inhibited cathepsin S with Ki = about 10-10 M to 10-4 M.

IT **330473-80-8P 330473-81-9P 330474-04-9P**
330474-09-4P 330474-26-5P 330474-81-2P
330475-40-6P 330475-41-7P 330475-58-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amino acid cyanomethyl amides as cathepsin S inhibitors)

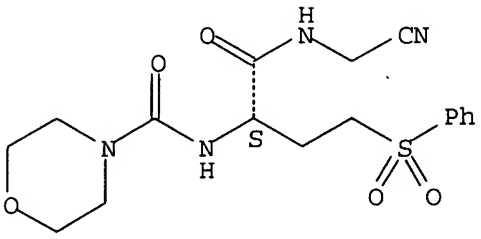
RN 330473-80-8 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-[[2-(trifluoromethoxy)phenyl]sulfonyl]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



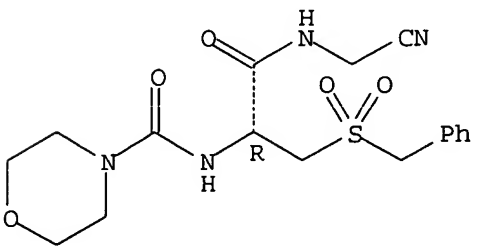
RN 330473-81-9 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-(phenylsulfonyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 330474-04-9 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1R)-2-[(cyanomethyl)amino]-2-oxo-1-[[(phenylmethyl)sulfonyl]methyl]ethyl]- (9CI) (CA INDEX NAME)

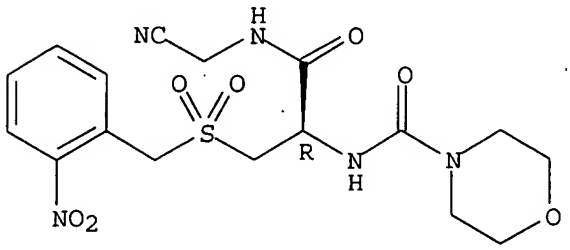
Absolute stereochemistry.



RN 330474-09-4 CAPLUS

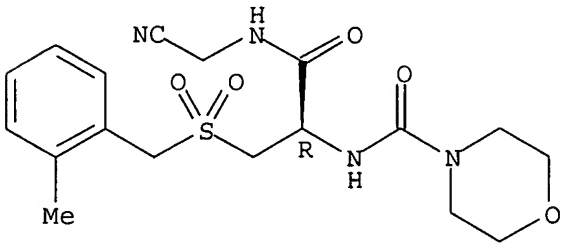
CN 4-Morpholinecarboxamide, N-[(1R)-2-[(cyanomethyl)amino]-1-[[[(2-nitrophenyl)methyl]sulfonyl]methyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



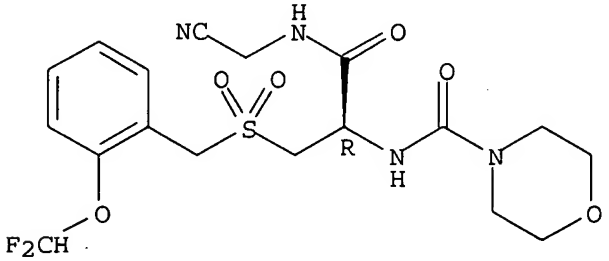
RN 330474-26-5 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1R)-2-[(cyanomethyl)amino]-1-[[[(2-methylphenyl)methyl]sulfonyl]methyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



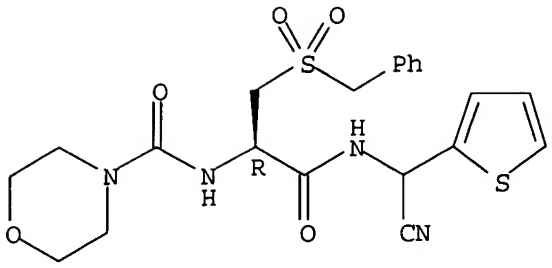
RN 330474-81-2 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1R)-2-[(cyanomethyl)amino]-1-[[[[2-(difluoromethoxy)phenyl]methyl]sulfonyl]methyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



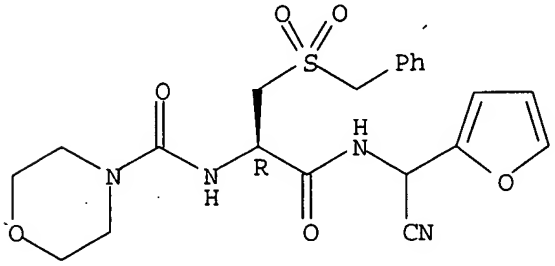
RN 330475-40-6 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1R)-2-[(cyano-2-thienylmethyl)amino]-2-oxo-1-[[(phenylmethyl)sulfonyl]methyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



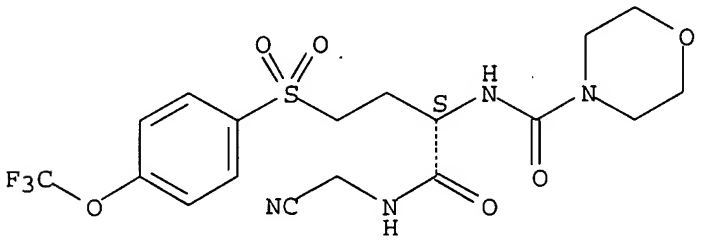
RN 330475-41-7 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1R)-2-[(cyano-2-furanylmethyl)amino]-2-oxo-1-[[(phenylmethyl)sulfonyl]methyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



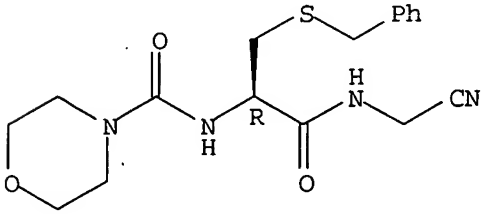
RN 330475-58-6 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-[[4-(trifluoromethoxy)phenyl]sulfonyl]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



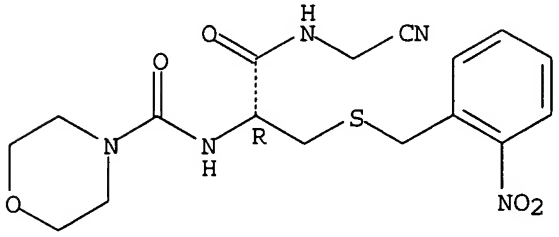
IT **294641-09-1P 294642-00-5P 330475-53-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of amino acid cyanomethyl amides as cathepsin S inhibitors)
RN 294641-09-1 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1R)-2-[(cyanomethyl)amino]-2-oxo-1-[[(phenylmethyl)thio]methyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



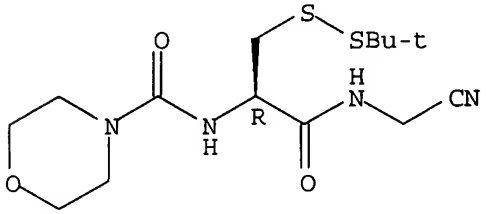
RN 294642-00-5 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1R)-2-[(cyanomethyl)amino]-1-[[[(2-nitrophenyl)methyl]thio]methyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 330475-53-1 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1R)-2-[(cyanomethyl)amino]-1-[[(1,1-dimethylethyl)dithio]methyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:666700 CAPLUS
DOCUMENT NUMBER: 133:252170
TITLE: Preparation of novel N-cyanomethyl amides as protease inhibitors
INVENTOR(S): Bryant, Clifford M.; Bunin, Barry A.; Kraynack, Erica A.; Patterson, John W.
PATENT ASSIGNEE(S): Axys Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 137 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000055125	A2	20000921	WO 2000-US6747	20000315
WO 2000055125	A3	20010426		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2368122	AA	20000921	CA 2000-2368122	20000315
BR 2000009042	A	20011226	BR 2000-9042	20000315
EP 1178958	A2	20020213	EP 2000-916343	20000315
EP 1178958	B1	20040218		
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TR 200103337	T2	20020321	TR 2001-200103337	20000315
TR 200103390	T2	20020521	TR 2001-200103390	20000315
US 6455502	B1	20020924	US 2000-526090	20000315
TR 200201874	T2	20021021	TR 2002-200201874	20000315
US 6476026	B1	20021105	US 2000-526485	20000315
JP 2002539191	T2	20021119	JP 2000-605556	20000315
EE 200100485	A	20030217	EE 2001-485	20000315
NZ 514234	A	20040227	NZ 2000-514234	20000315
AT 259782	E	20040315	AT 2000-916343	20000315
AU 774827	B2	20040708	AU 2000-37461	20000315
PT 1178958	T	20040730	PT 2000-916343	20000315
EP 1452522	A2	20040901	EP 2004-75486	20000315
EP 1452522	A3	20050209		
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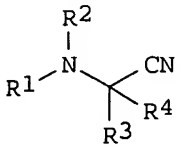
ZA 2001007494	A	20020911	ZA 2001-7494	20010911
ZA 2001007495	A	20020911	ZA 2001-7495	20010911
NO 2001004485	A	20011105	NO 2001-4485	20010914
BG 106003	A	20020628	BG 2001-106003	20011010
HR 2001000738	A1	20021231	HR 2001-738	20011012
US 2002086996	A1	20020704	US 2001-17851	20011214
US 6593327	B2	20030715		
US 2003096796	A1	20030522	US 2002-205600	20020724
HK 1044755	A1	20041217	HK 2002-105942	20020813
US 2003119788	A1	20030626	US 2002-241001	20020909
US 2004147745	A1	20040729	US 2004-758893	20040115
PRIORITY APPLN. INFO.:			US 1999-124420P	P 19990315
			EP 2000-916343	A3 20000315
			US 2000-526090	A1 20000315
			US 2000-526485	A3 20000315
			WO 2000-US6747	W 20000315
			US 2002-205600	B1 20020724

OTHER SOURCE(S): MARPAT 133:252170

GI



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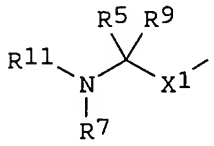
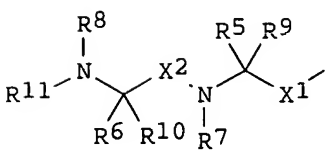
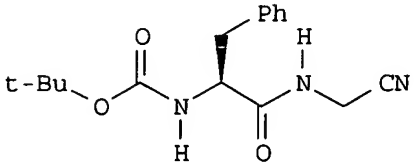


II



III



IV

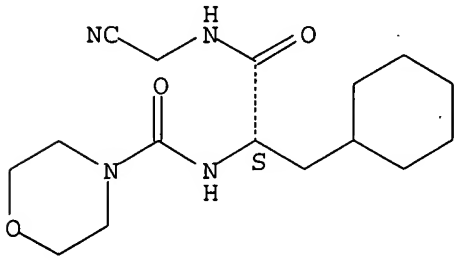
AB The title compds. [I; R1 = II, III (wherein X1, X2 = CO, CH2SO2; R5, R6 =

H, alkyl; R7, R8 = H, alkyl, etc.; R9, R10 = alkyl optionally substituted with CN, halo, NO2, etc.; R11 = X5X6R18; X5 = CO, COCO, SO2; X6 = a bond, O, NH, N(alkyl); R18 = alkyl optionally substituted with CN, halo, NO2, etc.); R2 = H, alkyl, etc.; R3 = H, alkyl, etc.; R4 = H, alkyl optionally substituted with CN, halo, NO2, etc.; R4 and R2 taken together form trimethylene, tetramethylene, phenylene-1,2-dimethylene, optionally substituted with hydroxy, oxo or methylene; R4 and R3 together with the carbon atom to which both are attached form cycloalkylene, heterocycloalkylene], useful for treating diseases associated with cysteine protease activity, particularly diseases associated with activity of cathepsins B, K, L or S such as inflammation and asthma, were prepared and formulated. Thus, reacting 2(S)-tert-butoxycarbonylamino-3-phenylpropionic acid with aminoacetonitrile.HCl in the presence of Et3N in DMF and MeCN afforded the amide (1S)-IV. Biol. data for compds. I were given.

IT **225120-04-7P 294641-09-1P 294641-99-9P**
294642-00-5P 294642-01-6P 294642-15-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of novel N-cyanomethyl amides as protease inhibitors)

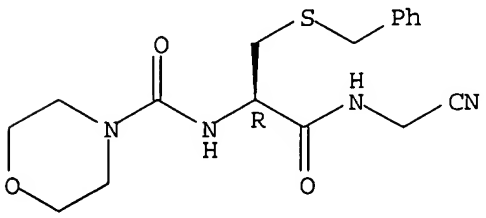
RN 225120-04-7 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-2-[(cyanomethyl)amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



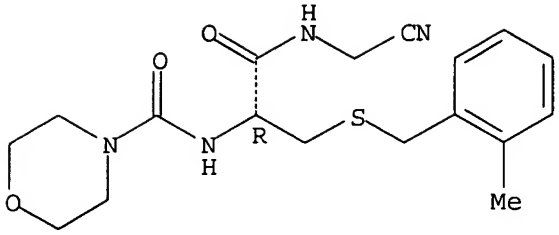
RN 294641-09-1 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1R)-2-[(cyanomethyl)amino]-2-oxo-1-[[(phenylmethyl)thio]methyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



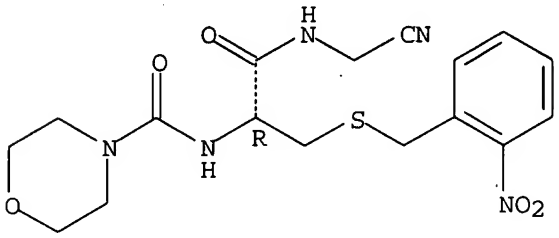
RN 294641-99-9 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1R)-2-[(cyanomethyl)amino]-1-[[[(2-methylphenyl)methyl]thio]methyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



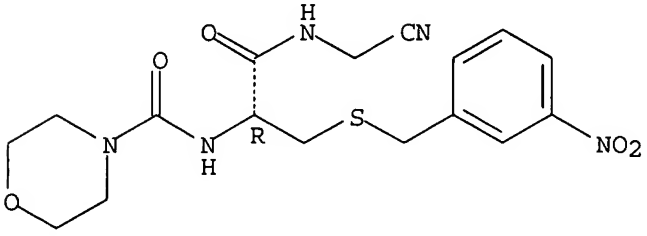
RN 294642-00-5 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1R)-2-[(cyanomethyl)amino]-1-[[[(2-nitrophenyl)methyl]thio]methyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



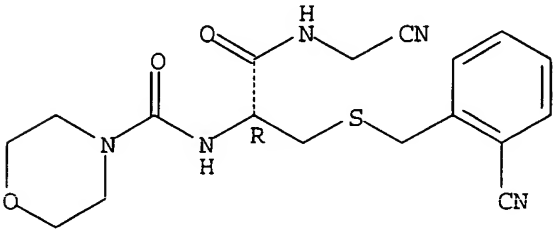
RN 294642-01-6 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1R)-2-[(cyanomethyl)amino]-1-[[[(3-nitrophenyl)methyl]thio]methyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 294642-15-2 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1R)-2-[(cyanomethyl)amino]-1-[[[(2-cyanophenyl)methyl]thio]methyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L5 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:628128 CAPLUS
DOCUMENT NUMBER: 133:208196
TITLE: Preparation of peptides as reversible inhibitors of

cathepsin S

INVENTOR(S): Cywin, Charles L.; Frye, Leah L.; Morwick, Tina; Spero, Denice M.; Thomson, David; Ward, Yancey

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 315 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000051998	A1	20000908	WO 1999-US26278	19991105
W: CA, JP, MX				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2360740	AA	20000908	CA 1999-2360740	19991105
EP 1159273	A1	20011205	EP 1999-973745	19991105
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6395897	B1	20020528	US 1999-434106	19991105
JP 2002538151	T2	20021112	JP 2000-602225	19991105
US 6608057	B2	20030819	US 2001-82952	20011024
US 2002091259	A1	20020711	US 2002-82952	20020224
US 2003158406	A1	20030821	US 2003-366282	20030213
US 6730671	B2	20040504		

PRIORITY APPLN. INFO.:		
US 1999-122570P	P	19990302
US 1999-434106	A1	19991105
WO 1999-US26278	W	19991105
US 2001-82952	A3	20011024

OTHER SOURCE(S): MARPAT 133:208196

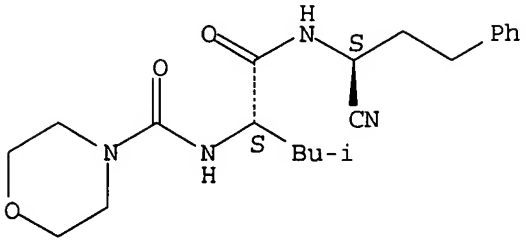
AB Compds. R1-A-NHCR2R3C(:X)NR4CR5R6R7 [A = C:O, C:S, C:NH or substituted imino group; R1 = (un)substituted alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, amino; R2, R4 = H, alkyl; R3, R6 = H or (un)substituted alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl; R5 = H, alkyl, cycloalkyl; R7 = R8C(Z), where Z = O, S, NH or substituted derivative and R8 is (un)substituted 5-8 membered monocyclic or 8-11 membered bicyclic heteroaryl having 1-4 heteroatoms selected from N, O and S; X = O, S, NOH] were prepared as cathepsin S inhibitors. Thus, morpholine-4-carboxylic acid [1-(S)-[1-(S)-cyano-3-phenylpropylcarbamoyl]-3-methylbutyl]amide was prepared by coupling L-homophenylalaninamide with N-(4-morpholinecarbonyl)-L-leucine and reaction with cyanuric chloride. Compds. of the invention were evaluated for inhibition of cathepsin S (IC50 ≤ 100 μM).

IT **290816-49-8P 290816-76-1P 290816-77-2P**
290816-78-3P 290816-79-4P 290816-81-8P
290816-82-9P 290816-83-0P 290816-84-1P
290816-85-2P 290816-86-3P 290816-87-4P
290816-88-5P 290816-89-6P 290816-91-0P
290816-92-1P 290816-93-2P 290816-94-3P
290816-95-4P 290816-96-5P 290816-97-6P
290817-01-5P 290817-02-6P 290817-03-7P
290817-07-1P 290817-08-2P 290817-10-6P
290817-11-7P 290817-12-8P 290817-14-0P
290817-15-1P 290817-17-3P 290817-18-4P
290817-19-5P 290817-20-8P 290817-21-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptides as reversible inhibitors of cathepsin S)

RN 290816-49-8 CAPLUS

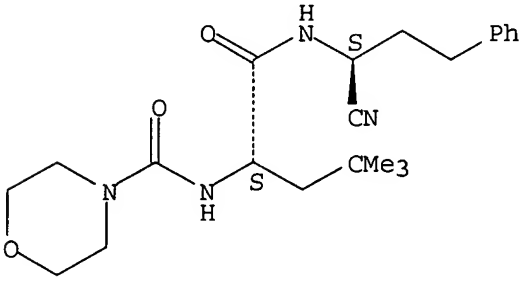
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyano-3-phenylpropyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



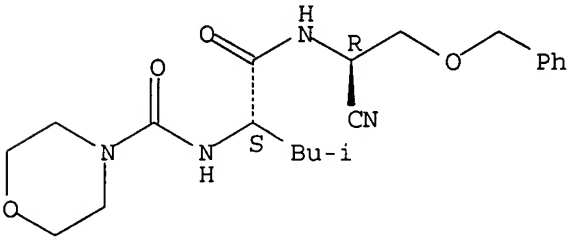
RN 290816-76-1 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyano-3-phenylpropyl]amino]carbonyl]-3,3-dimethylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



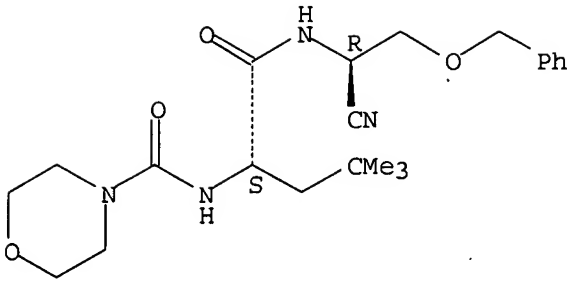
RN 290816-77-2 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-1-cyano-2-(phenylmethoxy)ethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



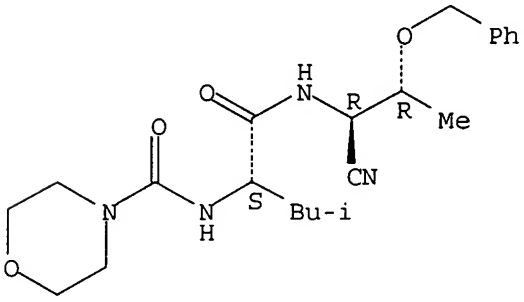
RN 290816-78-3 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-1-cyano-2-(phenylmethoxy)ethyl]amino]carbonyl]-3,3-dimethylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



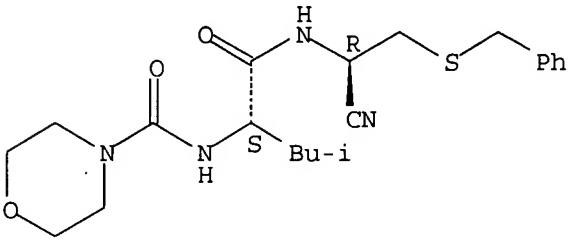
RN 290816-79-4 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R,2R)-1-cyano-2-(phenylmethoxy)propyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



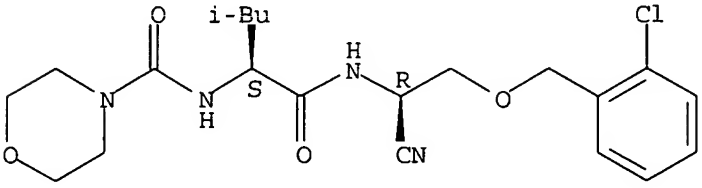
RN 290816-81-8 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-1-cyano-2-[(phenylmethyl)thio]ethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



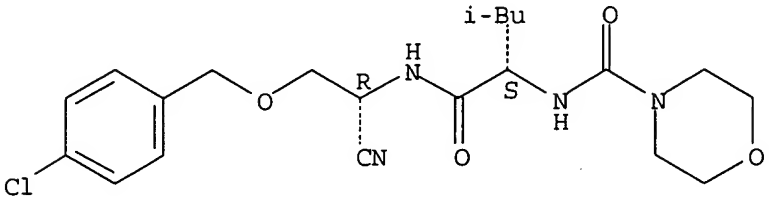
RN 290816-82-9 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-2-[(2-chlorophenyl)methoxy]-1-cyanoethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



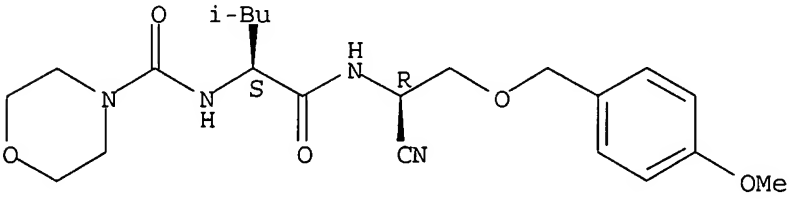
RN 290816-83-0 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-2-[(4-chlorophenyl)methoxy]-1-cyanoethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



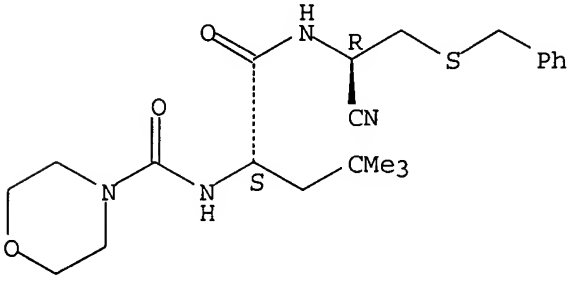
RN 290816-84-1 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-1-cyano-2-[(4-methoxyphenyl)methoxy]ethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



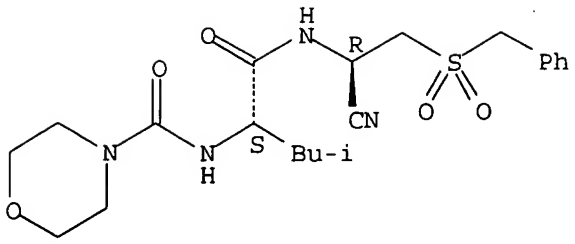
RN 290816-85-2 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-1-cyano-2-[(phenylmethyl)thio]ethyl]amino]carbonyl]-3,3-dimethylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



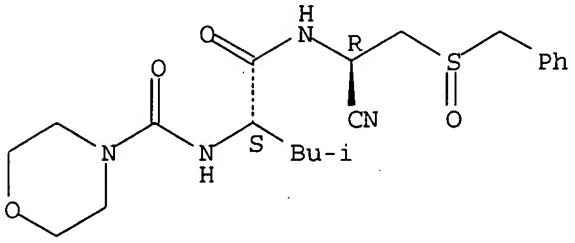
RN 290816-86-3 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-1-cyano-2-[(phenylmethyl)sulfonyl]ethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



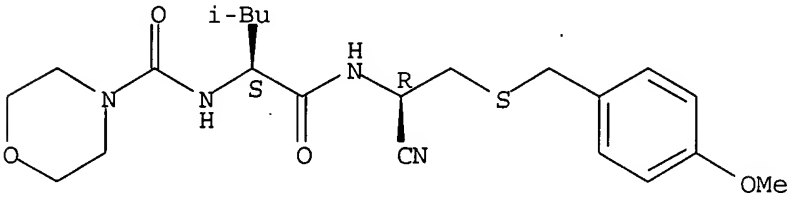
RN 290816-87-4 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-1-cyano-2-[(phenylmethyl)sulfinyl]ethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



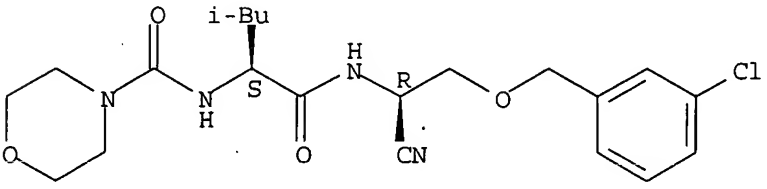
RN 290816-88-5 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-1-cyano-2-[[(4-methoxyphenyl)methyl]thio]ethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



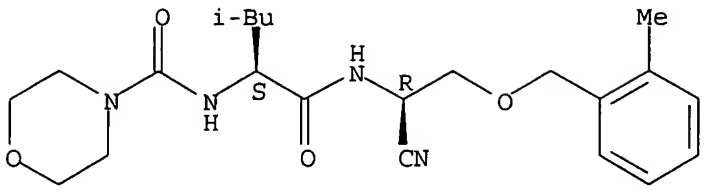
RN 290816-89-6 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-2-[(3-chlorophenyl)methoxy]-1-cyanoethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



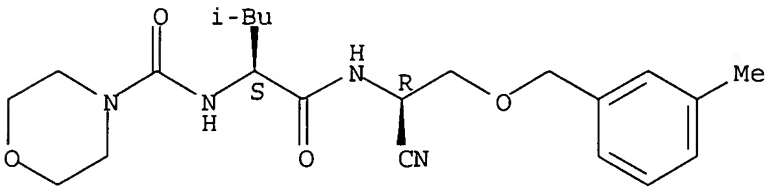
RN 290816-91-0 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-1-cyano-2-[(2-methylphenyl)methoxy]ethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



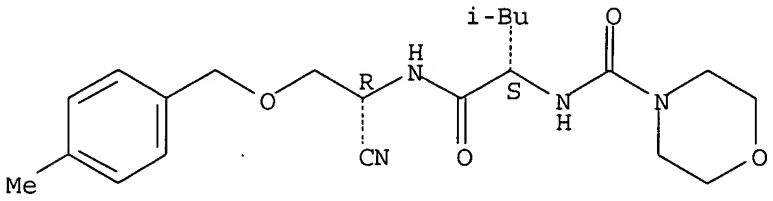
RN 290816-92-1 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-1-cyano-2-[(3-methylphenyl)methoxy]ethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



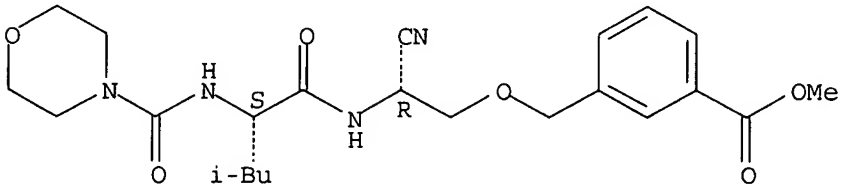
RN 290816-93-2 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-1-cyano-2-[(4-methylphenyl)methoxy]ethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



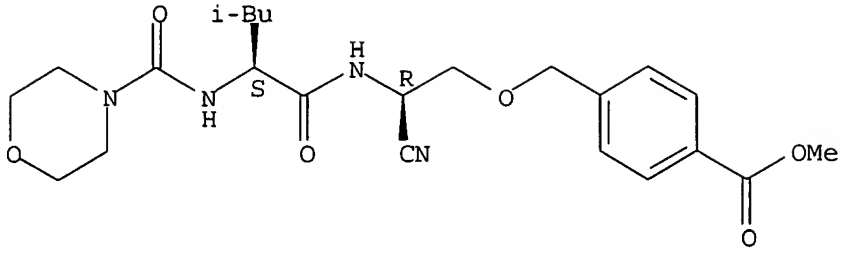
RN 290816-94-3 CAPLUS
CN Benzoic acid, 3-[[(2R)-2-cyano-2-[[(2S)-4-methyl-2-[(4-morpholinylcarbonyl)amino]-1-oxopentyl]amino]ethoxy]methyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



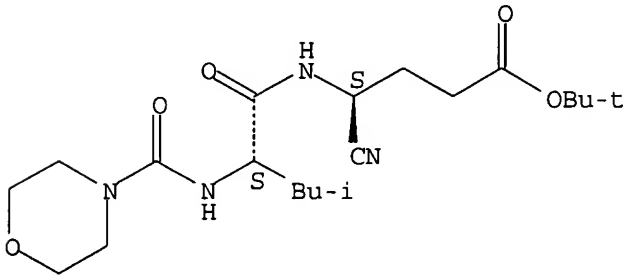
RN 290816-95-4 CAPLUS
CN Benzoic acid, 4-[[(2R)-2-cyano-2-[[(2S)-4-methyl-2-[(4-morpholinylcarbonyl)amino]-1-oxopentyl]amino]ethoxy]methyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



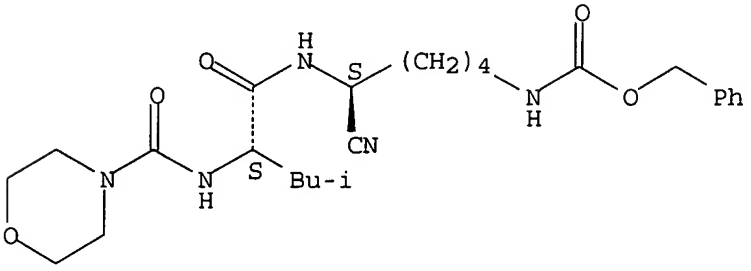
RN 290816-96-5 CAPLUS
CN Butanoic acid, 4-cyano-4-[[(2S)-4-methyl-2-[(4-morpholinylcarbonyl)amino]-1-oxopentyl]amino]-, 1,1-dimethylethyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



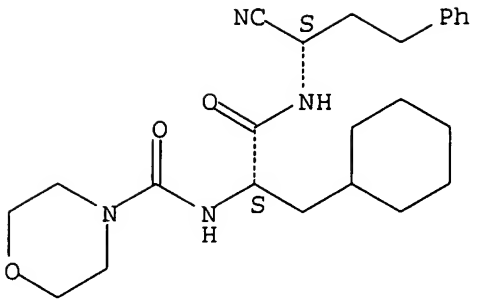
RN 290816-97-6 CAPLUS
CN Carbamic acid, [(5S)-5-cyano-5-[[(2S)-4-methyl-2-[(4-morpholinylcarbonyl)amino]-1-oxopentyl]amino]pentyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



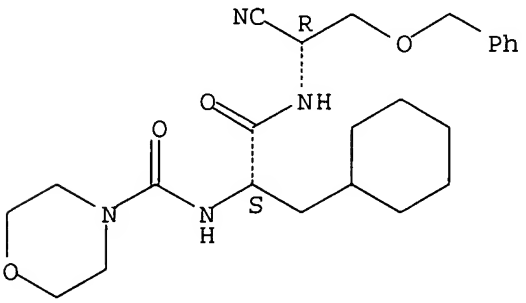
RN 290817-01-5 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-2-[[(1S)-1-cyano-3-phenylpropyl]amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



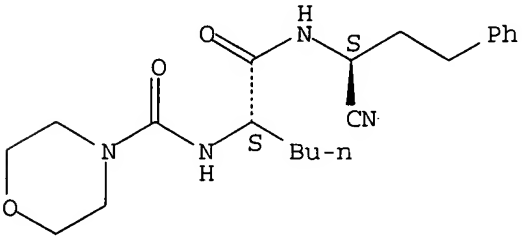
RN 290817-02-6 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-2-[[(1R)-1-cyano-2-(phenylmethoxy)ethyl]amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



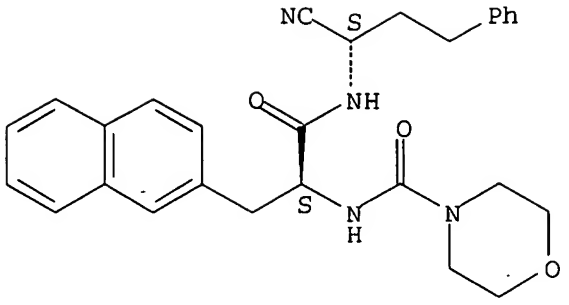
RN 290817-03-7 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyano-3-phenylpropyl]amino]carbonyl]pentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



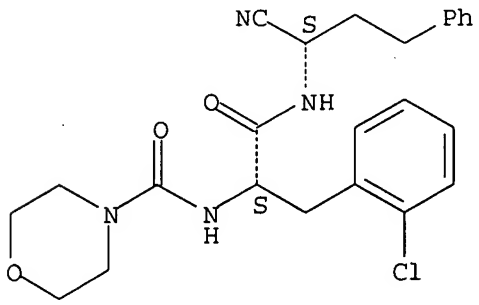
RN 290817-07-1 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-2-[[(1S)-1-cyano-3-phenylpropyl]amino]-1-(2-naphthalenylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



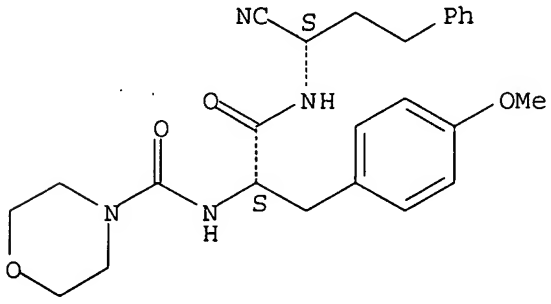
RN 290817-08-2 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[(2-chlorophenyl)methyl]-2-[[(1S)-1-cyano-3-phenylpropyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



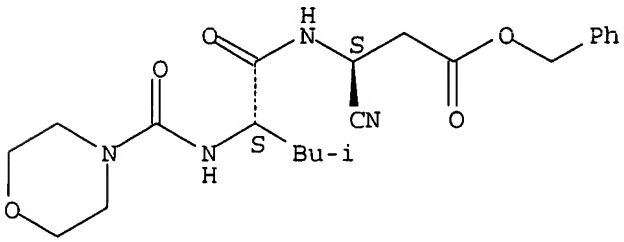
RN 290817-10-6 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-2-[[(1S)-1-cyano-3-phenylpropyl]amino]-1-[(4-methoxyphenyl)methyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



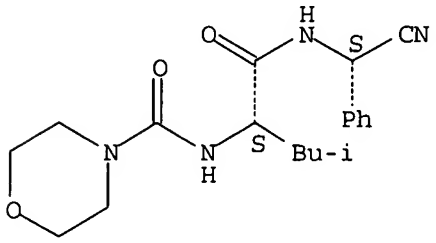
RN 290817-11-7 CAPLUS
CN Propanoic acid, 3-cyano-3-[[(2S)-4-methyl-2-[(4-morpholinylcarbonyl)amino]-1-oxopentyl]amino]-, phenylmethyl ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



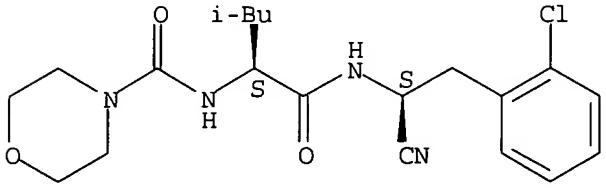
RN 290817-12-8 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(S)-cyanophenylmethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



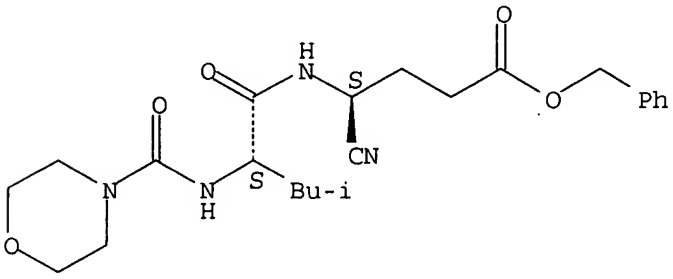
RN 290817-14-0 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-2-(2-chlorophenyl)-1-cyanoethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



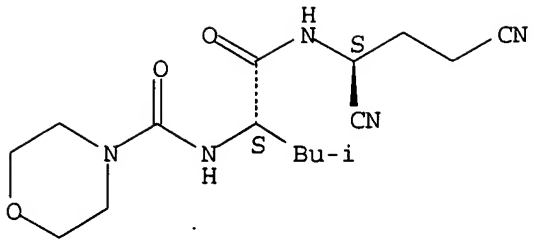
RN 290817-15-1 CAPLUS
CN Butanoic acid, 4-cyano-4-[[(2S)-4-methyl-2-[(4-morpholinylcarbonyl)amino]-1-oxopentyl]amino]-, phenylmethyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



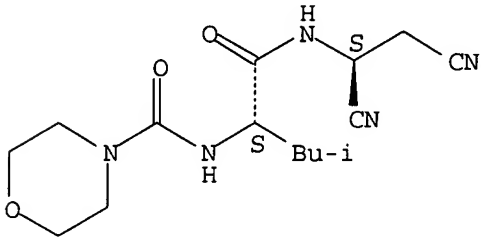
RN 290817-17-3 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1,3-dicyanopropyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



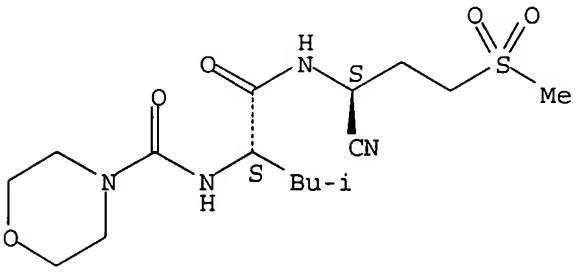
RN 290817-18-4 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1,2-dicyanoethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



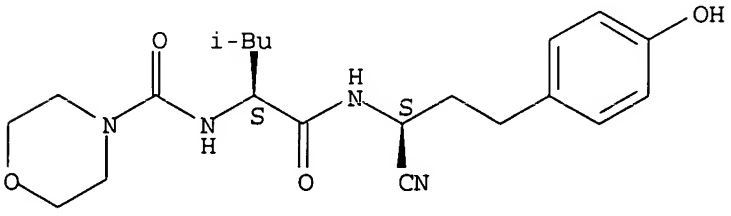
RN 290817-19-5 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyano-3-(methylsulfonyl)propyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 290817-20-8 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyano-3-(4-hydroxyphenyl)propyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

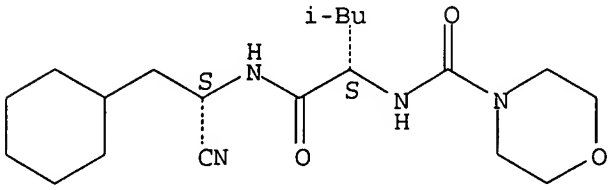
Absolute stereochemistry.



RN 290817-21-9 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyano-2-

cyclohexylethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:592709 CAPLUS
DOCUMENT NUMBER: 133:193494
TITLE: Preparation of di- and tripeptide nitrile derivatives as inhibitors of cathepsin L and cathepsin S
INVENTOR(S): Tucker, Howard; Large, Michael Stewart; Oldfield, John; Johnstone, Craig; Edwards, Philip Neil
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000049008	A1	20000824	WO 2000-GB529	20000216
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1155011	A1	20011121	EP 2000-903845	20000216
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002537294	T2	20021105	JP 2000-599748	20000216
PRIORITY APPLN. INFO.:			GB 1999-3853 A	19990220
			GB 1999-16099 A	19990710
			GB 1999-17171 A	19990723
			WO 2000-GB529 W	20000216

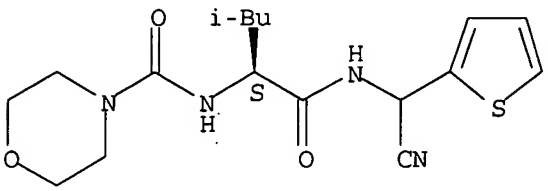
OTHER SOURCE(S): MARPAT 133:193494

AB Peptide nitriles R1-(AA1)n-AA2-NHCR2R3CN [n = 0 or 1; R1 = H, (un)substituted benzyl or acyl; R2 = H, (un)substituted alkyl, alkoxy, alkenyl, alkynyl, alkoxycarbonyl, carbamoyl, Ph, etc.; R3 = H, alkyl; AA1 and AA2 are certain amino acid residues] were prepared as cathepsin L or cathepsin S inhibitors. Thus, Cbz-Leu-Phe-NHCH(SPr-i)CN (Cbz = benzyloxycarbonyl), prepared by treating the amide with trifluoroacetic anhydride, showed IC50 = 38 nM for inhibition of cathepsin L.

IT **289062-09-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of di- and tripeptide nitrile derivs. as inhibitors of

cathepsin L and cathepsin S)
RN 289062-09-5 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[(cyano-2-thienylmethyl)amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:325961 CAPLUS
DOCUMENT NUMBER: 130:352553
TITLE: Synthesis of dipeptide nitriles as inhibitors of cysteine cathepsins
INVENTOR(S): Altmann, Eva; Betschart, Claudia; Gohda, Keigo; Horiuchi, Miyuki; Lattmann, Rene; Missbach, Martin; Sakaki, Junichi; Takai, Michihiro; Teno, Naoki; Cowen, Scott Douglas; Greenspan, Paul David; McQuire, Leslie Wighton; Tommasi, Ruben Alberto; Van Duzer, John Henry
PATENT ASSIGNEE(S): Novartis AG, Switz.; Novartis-Erfindungen Verwaltungsgesellschaft mbH
SOURCE: PCT Int. Appl., 137 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9924460	A2	19990520	WO 1998-EP6937	19981103
WO 9924460	A3	19990902		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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AU 9914873	A1	19990531	AU 1999-14873	19981103
AU 751669	B2	20020822		
EP 1028942	A2	20000823	EP 1998-958887	19981103
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
BR 9813197	A	20000829	BR 1998-13197	19981103
TR 200001189	T2	20000921	TR 2000-200001189	19981103
JP 2001522862	T2	20011120	JP 2000-520468	19981103
RU 2201420	C2	20030327	RU 2000-114821	19981103
ZA 9810073	A	19990505	ZA 1998-10073	19981104
TW 527362	B	20030411	TW 1998-87118553	19981105
NO 2000002320	A	20000704	NO 2000-2320	20000502
US 6353017	B1	20020305	US 2000-643639	20000822

US 2004029814	A1	20040212	US 2003-342872		20030115
US 2004110806	A1	20040610	US 2003-694672		20031028
PRIORITY APPLN. INFO.:			GB 1997-23407	A	19971105
			US 1997-108160P	P	19971205
			US 1997-985973	A	19971205
			WO 1998-EP6937	W	19981103
			US 1998-186223	B1	19981104
			US 2000-643639	A1	20000822
			US 2002-54590	B1	20020122
			US 2003-342872	A1	20030115

OTHER SOURCE(S): MARPAT 130:352553

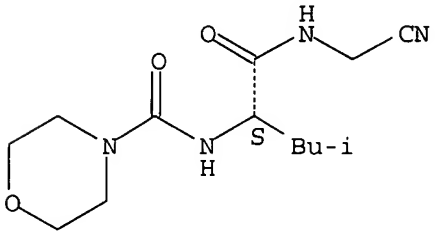
AB N-terminal substituted dipeptide nitriles R(L)xX1NHCR2R3C(:Y)NHCR4R5CN [R is optionally substituted aryl, alkyl, alkenyl, alkynyl, heterocyclyl; R2, R3 = H, optionally substituted alkyl, cycloalkyl, bicycloalkyl, or aryl-, biaryl-, cycloalkyl, bicycloalkylalkyl; R2 and R3 together represent alkylene, optionally interrupted by O, S, or NR6, where R6 is H, alkyl, arylalkyl; or R2 or R3 are linked by alkylene to the adjacent nitrogen to form a ring; R4, R5 = H, optionally substituted alkyl, arylalkyl, CO2R7, CONR7R8 (R7 is optionally substituted alkyl, aryl, arylalkyl, cycloalkyl, bicycloalkyl, or heterocyclyl and R8 is H or optionally substituted alkyl, aryl, arylalkyl, cycloalkyl, bicycloalkyl, heterocyclyl), etc.; R4 and R5 together represent alkylene, optionally interrupted by O, S, or NR6; X1 = CO, CS, SO, SO2, P(O)OR6; Y = O, S: L is optionally substituted Het, Het-CH2, CH2-Het (Het = O, N, or S); x = zero or 1] were prepared as inhibitors of cysteine cathepsins, e.g., cathepsins B, K, L and S, and can be used for the treatment of cysteine cathepsin dependent diseases and conditions. Thus, N-[2-[(3-carboxyphenyl)methoxy]-1(S)-cyanoethyl]-3-methyl-Nα-(2,2-diphenylacetyl)-L-phenylalaninamide was prepared and shown to have IC50 ≈ 5 nM for inhibition of cathepsin B.

IT **225119-70-0P 225120-04-7P 225121-07-3P**
225121-14-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis of dipeptide nitriles as inhibitors of cysteine cathepsins)

RN 225119-70-0 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

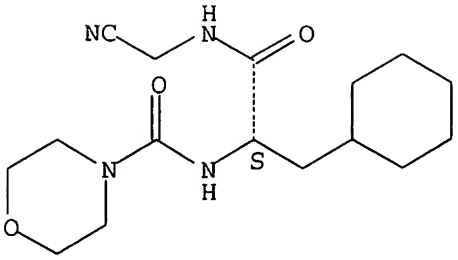
Absolute stereochemistry.



RN 225120-04-7 CAPLUS

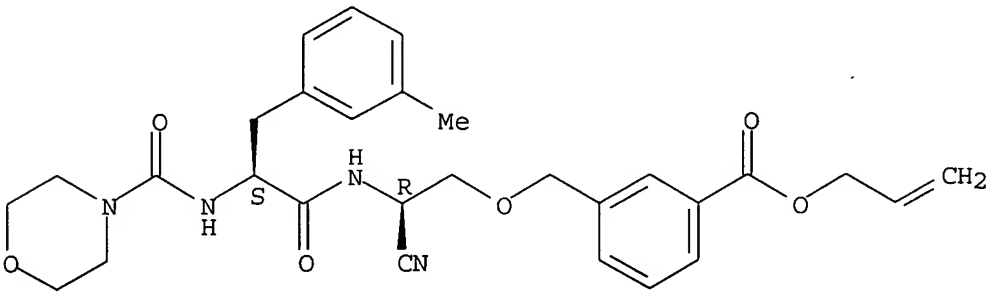
CN 4-Morpholinecarboxamide, N-[(1S)-2-[(cyanomethyl)amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



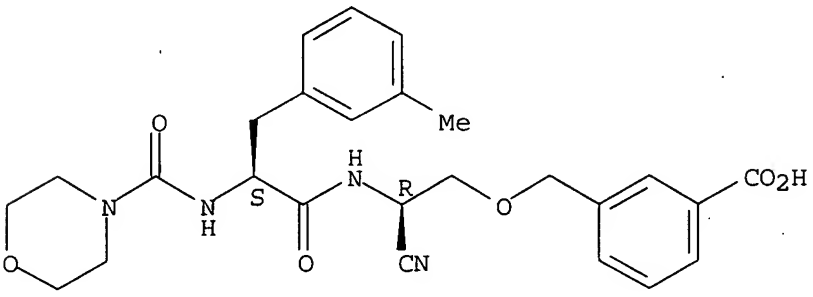
RN 225121-07-3 CAPLUS
CN Benzoic acid, 3-[[(2R)-2-cyano-2-[[(2S)-3-(3-methylphenyl)-2-[(4-morpholinylcarbonyl)amino]-1-oxopropyl]amino]ethoxy]methyl]-, 2-propenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 225121-14-2 CAPLUS
CN Benzoic acid, 3-[[(2R)-2-cyano-2-[[(2S)-3-(3-methylphenyl)-2-[(4-morpholinylcarbonyl)amino]-1-oxopropyl]amino]ethoxy]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	44.91	211.05
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-6.57	-6.57

STN INTERNATIONAL LOGOFF AT 15:19:23 ON 03 MAR 2005